UCSF

UC San Francisco Previously Published Works

Title

The neurobiology of openness as a personality trait.

Permalink

https://escholarship.org/uc/item/4b4985np

Authors

Abu Raya, Maison Ogunyemi, Adedoyin Broder, Jake et al.

Publication Date

2023

DOI

10.3389/fneur.2023.1235345

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at https://creativecommons.org/licenses/by/4.0/

Peer reviewed





OPEN ACCESS

EDITED BY Ian Robertson, Trinity College Dublin, Ireland

REVIEWED BY

Emanuele Raffaele Giuliano Plini, Trinity College Institute of Neuroscience, Ireland Mack Shelley, Iowa State University, United States

*CORRESPONDENCE

Maison Abu Raya ⊠ maison.aburaya@gbhi.org; ⊠ maison.aburaya@ucsf.edu

RECEIVED 06 June 2023 ACCEPTED 27 July 2023 PUBLISHED 14 August 2023

CITATION

Abu Raya M, Ogunyemi AO, Broder J, Carstensen VR, Illanes-Manrique M and Rankin KP (2023) The neurobiology of openness as a personality trait. *Front. Neurol.* 14:1235345. doi: 10.3389/fneur.2023.1235345

COPYRIGHT

© 2023 Abu Raya, Ogunyemi, Broder, Carstensen, Illanes-Manrique and Rankin. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

The neurobiology of openness as a personality trait

Maison Abu Raya^{1,2}*, Adedoyin O. Ogunyemi^{1,3}, Jake Broder¹, Veronica Rojas Carstensen¹, Maryenela Illanes-Manrique^{1,4} and Katherine P. Rankin^{1,2}

¹Global Brain Health Institute, University of California, San Francisco, San Francisco, CA, United States, ²Memory and Aging Center, Department of Neurology, Weill Institute for Neurosciences, University of California, San Francisco School of Medicine, San Francisco, CA, United States, ³Department of Community Health and Primary Care, University of Lagos, Lagos, Nigeria, ⁴Neurogenetics Research Center, Instituto Nacional de Ciencias Neurologicas, Lima, Peru

Openness is a multifaceted behavioral disposition that encompasses personal, interpersonal, and cultural dimensions. It has been suggested that the interindividual variability in openness as a personality trait is influenced by various environmental and genetic factors, as well as differences in brain functional and structural connectivity patterns along with their various associated cognitive processes. Alterations in degree of openness have been linked to several aspects of health and disease, being impacted by both physical and mental health, substance use, and neurologic conditions. This review aims to explore the current state of knowledge describing the neurobiological basis of openness and how individual differences in openness can manifest in brain health and disease.

KEYWORDS

Big Five model of personality, openness, dogmatism, cognitive flexibility, neurobiology

Introduction

Openness is one of the major personality traits derived from the Big Five model, which is a widely accepted framework for understanding personality that also includes the factors conscientiousness, extraversion, agreeableness, and neuroticism. Openness is characterized by a person's tendency to seek out new experiences and to be willing to explore ideas, values, emotions, and sensations that differ from their previous experience or established preferences (1). This trait has been extensively studied in the field of personality psychology and has been associated with a variety of positive outcomes, such as increased creativity, curiosity, adaptability, mental flexibility, and acceptance of others (2).

For instance, openness can boost creativity because individuals who score high in openness tend to be more imaginative and original in their thinking and, thus, are more likely to be receptive to new and unconventional ideas, which in turn can inspire them to think outside the box and come up with innovative solutions to problems (3). Research has shown that greater openness is directly associated with enhanced creative achievement (4). Openness is also related to mental flexibility, which refers to the ability to adapt one's thinking and behavior to better fit with changing situations and contexts. Individuals who are high in openness tend to be more adaptable, allowing them to navigate uncertain and complex situations with greater ease (5). Trait openness is also connected to more effective, innovative, and ethical leadership because studies have shown that open leaders are more likely to be receptive to feedback and new information, have better critical thinking and quicker problem-solving capabilities, make better decisions, and be more empathically responsive to the needs and mistakes of their followers (6, 7).

Openness as a personality trait has been widely studied in cultural and organizational psychology as well (8). While trait openness correlates with individuals' career advancement into managerial and professional roles (9), studies show that individuals who score high in openness are better able to manage conflicting cultural values and adapt to new cultural contexts, which is a crucial factor underlying success in multicultural organizations and environments. Openness has also been associated with various positive outcomes in professional settings, including better job performance, organizational citizenship behavior (10), and intercultural competence (11).

Measuring openness

Studies have generally used one of two approaches for measuring openness: standardized self- and other-report questionnaires, or direct neuropsychological measures in which openness is conceptualized to overlap with creativity and thus is measured via the volume and quality of creative output.

Typical questionnaire measures of openness ask individuals to rate themselves on a series of items related to their openness to new experiences, ideas, and ways of thinking (12). One of the most comprehensive standard questionnaires for assessing openness is the NEO personality inventory (NEO-PI) (13), which is a popular personality assessment tool that measures the "Big Five Personality Traits" including trait openness. This tool was developed by McCrae and Costa and was first published in 1978 (1). Over the years, they have published three updated versions of the inventory, with the latest being the NEO PI-3 in 2005 (13-15). It measures openness via 68-item subscale facet scores addressing openness to fantasy, aesthetics, feelings, actions, ideas, and values. The fantasy facet refers to the individual's level of imagination, creativity, and tendency to indulge in daydreams. The aesthetics facet assesses the individual's appreciation of art, music, and beauty. The feelings facet refers to the individual's emotional awareness, sensitivity, and tendency to experience deep and intense emotions. The actions facet refers to the individual's level of adventurousness, willingness to take risks, and preference for novelty. The ideas facet assesses the individual's level of intellectual curiosity, open-mindedness, and appreciation for new ideas. Lastly, the values facet refers to the individual's level of openness to alternative belief systems, such as spiritual or religious beliefs (14).

Another commonly used measure of openness is the HEXACO personality inventory (16), developed by Lee and Ashton in the early 2000s as an alternative to the NEO PI-R. It measures six broad dimensions of personality: honesty-humility, emotionality, extraversion, agreeableness, conscientiousness, and openness to experience. The HEXACO model differs from the NEO PI-R in that it includes the honesty-humility dimension and places a greater emphasis on the ethical and moral aspects of openness. The inventory has been revised to improve the psychometric properties of the measure, resulting in the 100-item HEXACO-PI-R in 2018 (4, 17, 18).

The California psychological inventory (CPI) is a personality inventory developed by Gough and Bradley in the 1950s, currently in its most recent version being the CPI-434, which was released in 2005 (19). The CPI is a self-report assessment tool that measures personality traits on 20 scales, including dominance, sociability, responsibility, self-control, and tolerance. The California psychological inventory (CPI) does not have a specific scale for openness; however, the CPI

does assess several dimensions investigators have argued are conceptually related to openness, including intellectual efficiency, creativity, and aesthetic appreciation (20).

Another widely used method for measuring openness is through creativity tests that include mental tasks which require individuals to think in unconventional ways. For example, the torrance tests of creative thinking (TTCT) was created by Torrance in the late 1950s and has been studied longitudinally for more than five decades to further validate the test across all age groups (21). This composite test assesses figural and verbal creativity using various subscales such as fluency, originality, elaboration, abstractness of thought, resistance to premature closure, and flexibility, which are based on the performance of different tests that need divergent thinking and other problemsolving skills (22). These tasks are designed to elicit imaginative and original responses from participants, and many of them involve generating alternative uses of objects, making associations between seemingly unrelated items, or imagining hypothetical scenarios (22). Additional examples of these types of "challenge" tasks include the alternative uses task (AUT) (22), the remote associates test (RAT) (23, 24), and the consequence task (25, 26), all of which require individuals to engage in divergent thinking, making distant associations and generating consequences for unlikely or impossible events.

The neurobiological basis of openness in neurologically healthy persons

Studies have used a mixed array of neuroimaging techniques in conjunction with these personality inventories with the goals of localizing the neural networks responsible for shaping openness as a personality trait, and developing better insight into the cognitive mechanisms that anchor openness neurobiologically. The majority of studies have sought to establish a correlation between scores on these measures and different brain regions by examining specific patterns of brain structure and function or neurochemical activity in individuals measured to have different levels of openness. Neuroimaging techniques such as structural magnetic resonance imaging (sMRI), resting-state functional MRI (rsfMRI), magnetic resonance spectroscopy (MRS), single photon emission computed tomography (SPECT), and positron emission tomography (PET) have each provided insights into the neurobiological basis of openness via this group comparison approach. A smaller set of studies have attempted to examine openness through task-based neuroimaging methods such as fMRI, in which participants were asked to perform a task in the scanner that the investigators construed as reflecting cognitive or emotional openness, such as the TTCT, AUT, or RAT. This research design might be less directly applicable to understanding openness as a personality trait but may still shed light on the specific neurobiology of cognitive processes known to contribute to openness, such as creativity and mental flexibility (22, 27-30).

Together, these studies have demonstrated distinct patterns of brain structure, connectivity, and activity, as well as neurochemical correlates, in brain regions known to be associated with creativity, abstraction, and cognitive flexibility. Broadly, the neurobiology of openness seems to be supported by three main functions and their corresponding neural networks: (1) reward processing, including the dopaminergic system along with ventromedial frontal and limbic reward networks, (2) the capacity to identify others'

perspectives and distinguish them from one's own, which is supported by the brain's default mode network, and (3) higher-order reasoning and decision-making, which is mediated by the executive frontoparietal control network (ECN). Evidence suggests that higher connectivity and functional integration among these three systems predicts trait openness. A summary of findings from neuroimaging studies across different methodologies is shown in Table 1.

Structural neuroimaging studies

The correlation between regional brain volumetrics and openness in healthy individuals has been examined in several studies with varying results. While some structural neuroimaging studies have found no relationship between openness and cortical brain volume (31), others have implicated a diverse set of structures. DeYoung and colleagues found that individuals who score high in openness tend to

TABLE 1 Summary of neuroimaging studies on trait openness.

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
DeYoung et al. (2010)	116 healthy individuals	NEO-PI-R ²	sMRI¹ Whole brain volumes and ROIs³ (voxel-level) expansion or contraction compared to the reference image	There were no discernible correlations between openness and local brain volume One cluster in the right parietal cortex was linked to this feature but was too small to cross the cluster-size criteria (2)
Riccelli et al. (2017)	507 healthy participants from the human connectome study	NEO-FFI ⁴	sMRI¹ SBM⁵	Greater area and folding in the prefrontal-parietal regions and a thinner cortex were associated with openness. These results show a relationship between individual variance in the sociocognitive dispositions outlined by the FFM and anatomical variability in prefrontal cortices (30)
Bjørnebekk et al. (2012)	265 healthy individuals	NEO-PI-R² BDI ⁶ WASI ⁷	sMRI¹ Multimodal imaging approach: regional analysis of cortical morphometry and white matter DTI⁵	The personality trait most directly connected to brain shape was neuroticism Greater neuroticism was linked to decreased total brain volume, extensive WM microstructure loss, and reduced frontotemporal surface area The inferior frontal gyrus was narrower in people with higher extraversion ratings, and the temporoparietal junction was adversely correlated with conscientiousness There were no conclusive links between agreeableness and openness and brain anatomy (31)
Wenfu Li et al. (2015)	246 college students	NEO-PI-R ² RAPM ⁹ WCAT ¹⁰	sMRI¹ VBM¹¹	These findings suggest that an individual's trait creativity may be significantly influenced by the specific personality trait of openness to experience and that creativity and the appropriate pMTG volume are related through openness to experience to some extent (34)

(Continued)

TABLE 1 (Continued)

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
Yasuno et al. (2017)	37 healthy participants	NEO-FFI ⁴	sMRI¹ VBM¹¹	Variations in intra-cortical myelination in the anterior cingulate/medial frontal cortex, posterior cingulate cortex, and posterior insula/adjacent putamen are related to individual differences in openness to experience These results support the theory that myelination serves as a biological underpinning for the trait of openness and plays a role in the relationship between creativity and mental illnesses (32)
Marstrand-Joergensen et al. (2021)	295 unique healthy individuals	NEO-PI-R ²	¹² rsfMRI Resting-state functional connectivity	Openness, including the fantasy component, was inversely correlated with DMN functional connectivity in the resting state (35)
Wang et al. (2022)	376 healthy participants	NEO-PI-R ² Creativity tasks: ¹³ CAQ, ¹⁴ CBI, ¹⁵ BICB Divergent thinking tasks: ¹⁶ PIT, ¹⁷ AUT, ¹⁸ UST	12rsfMRI Specific networks functional connectivity analysis Including the dorsal and ventral attention network, default mode network, limbic network, control network, and two others for somatosensory and visual networks	At the behavioral level, there is a correlation between creative achievement and both experiential openness and diverse thinking. Both openness to new experiences and divergent thinking involves the attentat networks and the default mode network since they both call for focus and the capacity for spontaneous thought (27)
Sun et al. (2019)	29 healthy university students	² NEO-PI-R Divergent thinking tasks: ¹⁷ AUT, ¹⁹ OCT (as a control task)	Task-fMRI Activation functional connectivity analysis	Different combinations of network connectivity patterns predict creativity and openness to experience Positive connections between the precuneus and supramarginal gyrus and the middle frontal gyrus/ superior frontal gyrus were found Individual difference analysis showed a significant correlation between openness to experience and the intensity of functional connectivity between various important default mode, cognitive control, and salience network areas The network-based mechanisms that underlie creativity and the neurological foundation of individual differences in openness to experience were found to be true (54)

(Continued)

TABLE 1 (Continued)

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
Wei et al. (2014)	269 healthy individuals	Divergent thinking: measured by the torrance tests of creative thinking	Pre- and post-task—resting state fMRI Whole-brain voxel-based activity and ROI-functional connectivity	Study findings suggest that increased RSFC between the default mode network's mPFC and mTG may be essential for creativity and that cognitive stimulation can increase RSFC between these two brain regions (reflecting creativity training-induced changes in functional connectivity, especially in the lower creativity individuals who had lower scores of torrance tests of creative thinking) (55)
Beaty et al. (2018)	163 healthy adults	Creative ideation task, alternate uses task (AUT) of divergent thinking	Two task-based fMRI samples and one task-free resting-state sample fMRI during creative ideation task Functional connectivity analysis	Greater default mode network, SN, and ECN functional connectivity are associated with higher creativity and divergent thinking (56)

A summary of findings and methodology from neuroimaging studies showing correlational structural and functional connectivity and activity to variability in openness and creativity and divergent thinking as another aspect of trait openness. We conducted a comprehensive literature search using the PubMed database for studies published from 1979 to 2023 in peer-reviewed journals that investigated the neurobiological correlates of openness. We included original articles that reported brain imaging data or neurophysiological measures of brain function in relation to measures of openness. Here we review the most recent relevant neuroimaging studies. ¹Structural MRI (sMRI), ²Revised NEO personality inventory (NEO-FI-R) (57), ³Region of interest (ROI), 4NEO-five-factors-inventory (NEO-FI-R) (13), ⁵Surface-based morphometry (SBM), 68bck depression inventory (BDI) (58), 7Vechsler abbreviated scale of intelligence (WASI) (59), 8Diffusion tensor imaging (DTI), ³Raven's advanced progressive matrix (RAPM) (60), 10The creativity assessment packet (WCAT) (61), 11Voxel-based morphometry (VBM), 12Resting-state functional magnetic resonance imaging (rsfMRI), 13The creative achievement questionnaire (CAQ) (62), 14Creative behavior inventory (CBI) (63), 15The biographical inventory of creative behaviors (BICB) (64), 16The product improvement task (PIT), 17The alternate uses task (AUT) (21), 18The utopian situations task (UST), 19Object characteristics task (OCT).

have a larger prefrontal cortex, which is the part of the brain responsible for higher-order thinking, decision-making, and planning (2). They also found an association with the volume of the inferior parietal lobule, which is linked with working memory, attention control, and general intelligence, suggesting that these cognitive processes might be associated with openness (2).

Openness has also been associated with increased gray matter volume in the anterior cingulate cortex (ACC), which is involved in emotion regulation and conflict monitoring (32).

Another neuroimaging study of healthy older adults from the Baltimore longitudinal study of aging found that higher openness was associated with increased gray matter volume in the frontopolar cortex. These regions are involved in cognitive control and executive function (33, 34), and enable individuals with higher openness to hold alternative actions in working memory in order to evaluate new options and ideas (33). The same study showed negative correlations between openness and volume in the right ventromedial prefrontal (vmPFC) and left fronto-insular cortex, regions that are involved in evaluation of negative outcomes and are linked to inhibitory or cautionary reactions to unpleasant or threatening stimuli. These data suggest that people with higher trait openness might be less vulnerable to such inhibitory reactions, while individuals with higher levels of anxiety are less likely to engage in cognitive or behavioral openness due to perceived risk (33, 35).

Functional connectivity studies

Two networks, in particular, appear in the majority of functional connectivity studies of creativity. The first, typically called the default mode network (DMN), includes the posterior cingulate cortex (PCC), dorsomedial prefrontal cortex (dmPFC), lateral parietal cortex, and hippocampal memory regions (33, 36). This network is involved in self-referential processing and social perspective-taking and is thought to be involved in a range of cognitive processes, including interpersonal perspective taking, introspection, and autobiographical memory (37). The second network relevant to trait openness is the executive control network (ECN), which comprises the dorsolateral prefrontal cortex (dlPFC) and the lateral posterior parietal cortex (PPC). It is an externally-oriented network involved in attentional selection, active task control, and executive functions, and is responsible for higher-order reasoning and decision-making. The dIPFC has also been implicated in the regulation of affect via reallocation of attention (36, 38).

Task-free functional imaging studies suggest that openness may be associated with increased functional connectivity *between* brain networks involved in cognitive control (i.e., the ECN) and self-referential processing (the DMN) (27). While higher levels of activity within the DMN have been found to predict lower trait openness, higher levels of connectivity between the DMN and ECN appear to allow individuals with higher levels of openness to better process

information, generate new ideas, and approach challenges in creative and innovative ways. This DMN-ECN connectivity pattern in individuals with higher levels of trait openness is also correlated with cognitive flexibility, allowing these individuals to switch between different mental sets and think outside the box (38). Furthermore, evidence from these studies suggests that connectivity of the DMN and ECN networks with the brain's reward regions (including the vmPFC, nucleus accumbens, and head of the caudate) allows individuals with higher trait openness to be better able to integrate diverse sources of emotional and cognitive information, and to have a greater propensity to turn self-reflection and introspection about emotionally salient ideas and experiences into creative action (35).

In otherwise neurologically healthy individuals, certain cognitive and behavioral approaches and personality traits can be maladaptive, even falling on the spectrum of psychopathology. Dogmatism, or fundamentalism, can be understood to represent the opposite of trait openness because it is characterized by rigid adherence to a set of ideas and the intentional exclusion of competing beliefs. Thus, studies of dogmaticism are relevant to the neurobiology of openness, and have important implications for the mechanisms of decision-making, problem-solving, and learning (28). Task-based fMRI studies have shown that individuals with high levels of mental rigidity exhibit lower activation in the vmPFC during tasks that require flexible thinking, such as set-shifting or task-switching, compared to individuals with high levels of mental flexibility (28, 39). Dogmatism has been found to be associated with decreased functional connectivity between the vmPFC and the temporoparietal junction (TPJ) (28), while ideologic openness is associated with increased functional connectivity between the vmPFC and the ACC, regions involved in error monitoring and motivation (28, 40, 41).

Neurochemistry

One of the key neural systems that has been implicated in trait openness is the dopaminergic mesolimbic pathway, which is involved in reward processing, motivation, and novelty-seeking behavior. Several lines of research have demonstrated that individuals high in openness exhibit greater activation in the ventral striatum, a key component of the mesolimbic reward pathway, during tasks that involve processing novel or unexpected information. Other studies showed that individuals who have a particular variant of the dopamine receptor gene (DRD4) tend to score higher in openness (42). The DRD4 gene has also been linked to sensation-seeking behavior and risk-taking (43, 44).

Similarly, the neurotransmitter serotonin is associated with emotion regulation, and individuals who have the long allele variant of the serotonin transporter gene (5-HTTLPR) tend to score higher in openness (45). The short allele variant of the 5-HTTLPR gene has also been linked to anxiety and depression (46), which are negatively correlated with trait openness. Studies have examined the relationship between openness and the serotonergic system using positron emission tomography (PET) with different serotonergic receptor-binding radioligands, but with varied results. Kalbitzer and colleagues showed that participants' scores on the NEO-PI-R openness scale, and particularly the two subscales openness to actions and openness to values, were negatively correlated with the [11C] DASB binding radioligand for 5-HTT in limbic areas including the caudate (47). The

authors suggested that because there was less serotonin available in these areas, the action of the remaining serotonin was potentiated, similar to the facilitation caused by antidepressant treatment with selective serotonin reuptake inhibitors (SSRIs). However, other PET studies using different serotonin ligands [5-HT2AR (48) and 5-HT4R (49)] to investigate trait openness found no significant neural associations.

Certain drugs, such as psychedelics (i.e., LSD and psilocybin, which are agonists for the 5-HT2AR serotonin receptor), have been shown to increase openness in some individuals (50, 51). fMRI studies have also shown altered DMN activity and connectivity (52) in individuals during psychedelic use. As described earlier, the DMN is involved in self-referential thinking and introspection, leading to better self-awareness and self-regulation, though heightened DMN activity alone corresponds with decreased openness (36). However, the pattern of brain activity induced by psychedelics is characterized by increased variability and decreased stability, which may in turn result in greater connectivity between the DMN and other networks. The authors posit that this leads to a "liberation" of cognitive and affective processes, allowing for increased creativity and divergent thinking as part of the trait openness (52).

Research using magnetic resonance spectroscopy (MRS) has also revealed that individuals with high levels of openness have higher levels of the neurotransmitter glutamate in anterior cingulate cortex (ACC) regions related to error monitoring and motivation, as well as in vmPFC reward areas (53). Glutamate is a key neurotransmitter involved in synaptic plasticity and learning, and these results suggest that increased glutamatergic activity in these reward and motivation areas in more open individuals may lead to a greater capacity for cognitive flexibility and learning (53).

Trait openness in neurologic disease

While the studies described thus far have included predominantly healthy individuals, additional insights about the neuroanatomical and neurochemical basis of openness can be derived from research models of neurological diseases as well. Lesion studies can shed light on which brain areas are both necessary and sufficient for particular behaviors and thought processes. Studying altered neural activity and connectivity in individuals with brain aging, injury, and disease who also show atypical levels of trait openness can facilitate our understanding of the underlying neural mechanisms.

Age-related cognitive decline

Studies have investigated how trait openness relates to aging as and age-related cognitive decline. Several investigations have found a negative correlation between openness and age (11, 15, 65); however, others showed that openness can have a protective effect against cognitive decline in middle-aged and older adults (66, 67) and correlates with better cognitive performance, social abilities, and wellbeing in older age (66, 68). Other research has suggested that openness may represent a behavioral channel to cognitive and social engagement, which are linked to a lower risk of dementia and cognitive decline (13, 69, 70).

Traumatic brain injury

Studies of individuals with severe structural brain lesions (28, 71), such as penetrating traumatic brain injury (pTBI) (28), show that they often exhibit an extreme lack of openness in the form of mental rigidity, dogmatism, and ideological or religious fundamentalism. Brain-behavior studies of these individuals' patterns of mental rigidity highlight the role of the vmPFC and its connectivity with other brain regions (28). In a study that included a large sample of patients with pTBI, Zhong and colleagues found that patients with injuries to the vmPFC scored higher than patients with dlPFC lesions on a standardized scale of religious fundamentalism, and that on average both groups showed abnormally high scores compared to neurologically healthy individuals. Analyses adjusting for the size of the lesions in the vmPFC suggested the interaction between vmPFC and dlPFC drove patients to have less cognitive flexibility and openness, again supporting the idea that the connection between reward- and executive-processing areas supports trait openness. This study gives insight into the role of both vmPFC and dlPFC in the revision of religious beliefs, suggesting that loss of cognitive flexibility is linked to an increase in fundamentalist belief adherence and resistance to novel information (28).

Neurodegenerative disease

The neurobiological mechanisms underlying changes in openness in individuals with neurodegenerative brain disease are complex and are still being elucidated. Similar to what has been observed in neurologically healthy individuals, studies in individuals with neurodegenerative disease have suggested that changes in the levels of dopamine, serotonin, and other neurotransmitters may play a role (54, 72). Additionally, the changes in frontal and temporal brain structure and connectivity often observed in patients with neurodegenerative disorders have been repeatedly linked to dysregulation and alteration of previously stable personality traits (73).

Several studies have suggested that individuals with neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD) may experience a decline in openness, particularly with respect to creativity and decision-making (74). Parkinson's disease is characterized by the degeneration of dopaminergic neurons in the substantia nigra that can lead to both motor and non-motor symptoms. Individuals with PD are more likely to have reduced openness to experience, the degree of which has been associated with the severity of motor symptoms and cognitive decline (75). In PD, atrophy in the vmPFC and dlPFC have been shown to impact both social cognition and decision-making, leading to a decrease in intellectual curiosity (76).

Notably, there is a growing evidence that some personality traits increase the likelihood of developing Alzheimer's disease and other dementias (77, 78). Several studies showed that openness, as a premorbid personality trait, was related to better cognitive outcomes in later life, suggesting that openness to experience contributes to cognitive reserve (79, 80). Openness also correlates with lower levels of aging-related hippocampal volume loss (81), and less Alzheimer's disease-related tau accumulation in the entorhinal cortex in cognitively healthy individuals (82). Tautvydaite and colleagues found that in a mixed group of individuals with and without AD-positive

biomarkers, premorbid openness predicted cognitive performance regardless of the individual's cognitive level, demographics, APOE&4 status, or CSF biomarker levels. They found that openness was the only personality domain from the five-factor model that contributed independently to cognitive performance (83). These findings imply that openness as a lifelong personality trait may play a protective role against age-related neuropathological processes (33, 79, 82).

Another neurodegenerative disorder that has been shown to directly impact trait openness is frontotemporal dementia (FTD). FTD is characterized by the degeneration of the frontal and temporal lobes of the brain, leading to changes in behavior, personality, and language (84). Research has shown that individuals with the behavioral variant FTD syndrome (bvFTD) have significantly lower scores on measures of openness compared to healthy controls (85, 86), and that this decline has been linked to neurodegeneration in regions including the vmPFC and ACC (87).

Mental rigidity and dogmatism are common symptoms of FTD, and can manifest in various ways. For example, many individuals with FTD exhibit perseveration, which is the repetition of the same behavior or thought despite changes in the environment. Studies suggest this behavior may be due to atrophy in the dIPFC and ACC, areas involved in cognitive flexibility and inhibitory control (88). Some patients may present with intense resistance to changes in their routine or environment, such as trying new foods, moving to a new residence, or wearing different clothes day to day. Again, studies have linked this with atrophy in the dIPFC and other brain regions that support cognitive flexibility and adaptive behavior (89). Other patients with FTD, particularly those with the right temporal or semantic variant of bvFTD (90), may hold rigid or inflexible beliefs and refuse to consider alternative viewpoints (91, 92). Evidence suggests this may be due to disruptions in the vmPFC, which is involved in making evaluations of rewards during decision-making (93, 94). Furthermore, disruptions in the white matter tracts connecting the dIPFC and other brain regions such as the insula and anterior cingulate cortex, correlate with cognitive inflexibility and dogmatism in FTD (95).

On the other hand, studies of individuals with FTD have also highlighted the relationship between openness and creativity, which can be unleashed in a subset of these patients. For instance, specific patients with bvFTD have been found to display enhanced creativity and divergent thinking in specific contexts such as artistic production (96–98). A subset of individuals with FTD may exhibit dramatically increased engagement in an artistically creative behavior, such as painting, drawing, or composing music, that was not present before the onset of the disease (85, 99). This enhanced creative production is thought to be related to changes in the brain network connectivity between the DMN and the salience network (SN) (95). This phenomenon has been referred to as "unleashed creativity" and may be related to changes in neural networks involved in the processing of semantic and emotional information (96).

An alternate theory to explain this phenomenon is that the loss of inhibitory control that occurs in FTD may release previously suppressed creative tendencies (100). Certain patterns of dysfunction in the vmPFC and dlPFC may lead to a shift in cognitive processing that favors creative thinking over other, more rigorous cognitive processes (99). Persons with FTD who show this unleashed creativity show greater atrophy in the left hemisphere of the brain, particularly in the ventral and dorsolateral frontal and temporal regions associated with social cognition, executive functioning, and semantic processing.

This atrophy appears to release inhibitions in the creative process, allowing for a more free-flowing expression of ideas and emotions (97, 99, 100), and thus, greater openness. Further research into this complex phenomenon in persons with FTD may provide new insights into the neural basis of openness and ultimately inform new strategies for the treatment and care of these individuals.

Conclusion

Openness is a complex construct that encompasses multiple dimensions, but examining the neurobiological basis of openness improves our understanding of the cognitive components of this personality trait. Structural, functional, and lesion studies converge to suggest that connectivity among specific brain networks supports trait openness; specifically, the interaction among (1) reward systems, mediated both by neurotransmitters like dopamine and serotonin and brain structures like the ventromedial prefrontal cortex (vmPFC); (2) frontal and parietal structures in the default mode network (DMN), supporting interpersonal perspective taking, self-reflection, and abstraction; and (3) dorsolateral prefrontal cortex (dlPFC) structures in the executive control network (ECN) that mediate cognitive flexibility and problem-solving. These three brain systems interact synergistically to support openness by increasing mental flexibility, reward responsiveness and novelty-seeking, and the ability to incorporate creativity into thought processes, decision-making, and behavior.

While creativity is typically associated with openness as a positive behavior, in some cases, it can also be associated with dysfunction or pathology. Reductions in openness are often seen in persons with brain disease and injury, particularly those affecting the frontal and temporal lobes. These changes are likely associated with alterations in neurotransmitter levels as well as brain structure and connectivity. The exact neurobiological mechanisms underlying unleashed creativity in FTD remain unclear, though disruptions in the frontotemporal networks critical for the integration of sensory, emotional, and cognitive information may lead to a breakdown in inhibitory processes that normally suppress creative expression, resulting in the emergence of novel and innovative ideas.

Clearly, further research is needed to understand the neuroanatomical basis of openness at a more granular level. With a richer and more precise understanding of the mechanisms underlying openness, better interventions could be developed to augment this highly positive trait, enhancing an individual's receptiveness to new experiences, ideas, perspectives, and values, and thus promoting many aspects of their brain health. From a policy interventional perspective, these links between brain health and openness suggest that fostering openness as a personality trait has the potential for far-reaching benefits across the lifespan on both personal and societal levels. Promoting openness within educational systems and workplaces can shape environments that nurture curiosity, creativity, and a willingness to embrace new ideas. Successful interventions could contribute to the development of individuals who are adaptable, innovative, and openminded, ultimately leading to better outcomes in education, workforce productivity, social cohesion, and personal brain health and mental well-being.

Author contributions

The manuscript benefited from the collective input of all authors during the conceptualization stage having all authors taking part in developing the ideas for this manuscript. KR and MR played a significant role in designing and structuring the paper. The initial draft was written by MR, who served as the first author, while the other coauthors contributed by reviewing and making edits. KR supervised the work and contributed to the writing, reviewing, and editing processes. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- 1. McCrae RR, Costa PT. Joint factors in self-reports and ratings: Neuroticism, extraversion and openness to experience. *Personality and Individual Differences*. (1983) 4:245–55. doi: 10.1016/0191-8869(83)90146-0
- 2. DeYoung CG, Hirsh JB, Shane MS, Papademetris X, Rajeevan N, Gray JR. Testing predictions from personality neuroscience. Brain structure and the big five. *Psychol Sci.* (2010) 21:820–8. doi: 10.1177/0956797610370159
- 3. Li W, Li X, Huang L, Kong X, Yang W, Wei D, et al. Brain structure links trait creativity to openness to experience. *Social Cognitive and Affective Neuroscience* [Internet]. (2015) 10:191–8. doi: 10.1093/scan/nsu041
- 4. Lee K, Ashton MC. Psychometric properties of the HEXACO-100. Assessment. (2018) 25:543–56.
- 5. Knaps A. Creativity and conflict resolution. Alternative pathways to peace, Defence Studies. (2015) 15:385–6. doi: 10.1080/14702436.2015.1093379
- 6. Hildenbrand K, Sacramento CA, Binnewies C. Transformational leadership and burnout: The role of thriving and followers' openness to experience. *Journal of occupational health psychology.* (2018) 23:31.
- 7. Iqbal Z, Abid G, Contreras F, Hassan Q, Zafar R. Ethical Leadership and Innovative Work Behavior: The Mediating Role of Individual Attributes. *Journal of Open Innovation Technology Market and Complexity.* (2020):6.
- 8. Çelik P, Storme M, Forthmann B. A new perspective on the link between multiculturalism and creativity: The relationship between core value diversity and divergent thinking. *Learning and Individual Differences [Internet]*. (2016) 52:188–96. Available from: https://www.sciencedirect.com/science/article/pii/S1041608016300127
- 9. Nieß C, Zacher H. Openness to experience as a predictor and outcome of upward job changes into managerial and professional positions. *PLoS One.* (2015) 10:e0131115. doi: 10.1371/journal.pone.0131115

- 10. Chiaburu DS, Oh IS, Berry CM, Li N, Gardner RG. The five-factor model of personality traits and organizational citizenship behaviors: a meta-analysis. *J Appl Psychol.* (2011) 96:1140–66. doi: 10.1037/a0024004
- 11. Schwaba T, Luhmann M, Denissen JJA, Chung JM, Bleidorn W. Openness to experience and culture-openness transactions across the lifespan. *J Pers Soc Psychol.* (2018) 115:118–36. doi: 10.1037/pspp0000150
- 12. Goldberg LR. An alternative "description of personality": The Big-Five factor structure. *Journal of Personality and Social Psychology.* (1990) 59:1216–29. doi: 10.1037/0022-3514.59.6.1216
- 13. Costa PT Jr, McCrae RR. Revised NEO Personality Inventory (NEO-PI-R) and NEO Five-Factor Inventory (NEO-FFI) professional manual. Odessa, FL: Psychological Assessment Resources (1992).
- 14. McCrae RR, Costa PT Jr, Martin TA. The NEO-PI-3: a more readable revised NEO Personality Inventory. J Pers Assess. (2005) 84:261–70. doi: 10.1207/s15327752 jpa 8403_05
- 15. McCrae RR, Costa PT Jr. Validation of the five-factor model of personality across instruments and observers. *J Pers Soc Psychol.* (1987) 52:81–90. doi: 10.1037//0022-3514.52.1.81
- 16. Lee K, Ashton MC. Psychometric Properties of the HEXACO Personality Inventory. *Multivariate Behavioral Research [Internet]*. (2004) 39:329–58. doi: 10.1207/s15327906mbr3902 8
- 17. Ashton MC, Lee K. Honesty-Humility, the Big Five and the Five-Factor Model. Journal of Personality. (2005) 73:1321–53. doi: 10.1111/j.1467-6494.2005.00351.x
- 18. Ashton MC, Lee K. Empirical, theoretical, and practical advantages of the HEXACO model of personality structure. *Pers Soc Psychol Rev.* (2007) 11:150–66. doi: 10.1177/1088868306294907
- 19. Gough HG, Bradley P. Cpi 260: Manual Consulting Psychologists Press (2005).
- 20. Gough H, Bradley P. CPI Manual. 3rd ed Consulting Psychologists Press (1996).
- 21. Torrance EP. Growing Up Creatively Gifted: The 22-Year Longitudinal Study. *The Creative Child and Adult Quarterly.* (1980) 3:148–58.
- 22. Torrance EP, Ball OE, Safter HT. Torrance Tests of Creative Thinking: Streamlined Scoring Guide for Figural Forms A and B; to be Used in Conjuction with the TTCT Norms-Technical Manual. Scholastic Testing Service; (2008).
- 23. Bowden EM, Jung-Beeman M. Normative data for 144 compound remote associate problems. *Behavior Research Methods, Instruments, & Computers [Internet].* (2003) 35:634–9. doi: 10.3758/BF03195543
- 24. Mednick SA. The associative basis of the creative process. *Psychological review*. (1962) 69:220–32.
- 25. Wilson RC, Guilford JP, Christensen PR, Lewis DJ. A factor-analytic study of creative-thinking abilities. *Psychometrika*. (1954) 19:297–311.
- 26. Torrance EP. Torrance tests of creative thinking. *Educational and Psychological Measurement.* (1966).
- 27. Wang X, Zhuang K, Li Z, Qiu J. The functional connectivity basis of creative achievement linked with openness to experience and divergent thinking. *Biol Psychol.* (2022) 168:108260. doi: 10.1016/j.biopsycho.2021.108260
- 28. Zhong W, Cristofori I, Bulbulia J, Krueger F, Grafman J. Biological and cognitive underpinnings of religious fundamentalism. *Neuropsychologia*. (2017) 100:18–25. doi: 10.1016/j.neuropsychologia.2017.04.009
- 29. Silvia PJ, Nusbaum EC, Berg C, Martin C, O'Connor A. Openness to experience, plasticity, and creativity: Exploring lower-order, high-order, and interactive effects. *Journal of Research in Personality [Internet]*. (2009) 43:1087–90. Available from: https://www.sciencedirect.com/science/article/pii/S0092656609001317
- 30. Riccelli R, Toschi N, Nigro S, Terracciano A, Passamonti L. Surface-based morphometry reveals the neuroanatomical basis of the five-factor model of personality. *Soc Cogn Affect Neurosci.* (2017) 12:671–84. doi: 10.1093/scan/nsw175
- 31. Bjørnebekk A, Fjell AM, Walhovd KB, Grydeland H, Torgersen S, Westlye LT. Neuronal correlates of the five factor model (FFM) of human personality: Multimodal imaging in a large healthy sample. *Neuroimage*. (2013) 65:194–208. doi: 10.1016/j. neuroimage.2012.10.009
- 32. Yasuno F, Kudo T, Yamamoto A, Matsuoka K, Takahashi M, Iida H, et al. Significant correlation between openness personality in normal subjects and brain myelin mapping with T1/T2-weighted MR imaging. *Heliyon [Internet]*. (2017) 3:e00411 Available from: https://www.sciencedirect.com/science/article/pii/S240584401731455X
- 33. Kapogiannis D, Sutin A, Davatzikos C, Costa P Jr, Resnick S. The five factors of personality and regional cortical variability in the Baltimore longitudinal study of aging. *Hum Brain Mapp.* (2013) 34:2829–40. doi: 10.1002/hbm.22108
- 34. Li W, Li X, Huang L, Kong X, Yang W, Wei D, et al. Brain structure links trait creativity to openness to experience, *Social Cognitive and Affective Neuroscience*, (2015) 10:191–198. doi: 10.1093/scan/nsu041
- 35. Marstrand-Joergensen MR, Madsen MK, Stenbæk DS, Ozenne B, Jensen PS, Frokjaer VG, et al. Default mode network functional connectivity negatively associated with trait openness to experience, Social Cognitive and Affective Neuroscience (2021) 16:950–61. doi: 10.1093/scan/nsab048

- 36. Heinonen J, Numminen J, Hlushchuk Y, Antell H, Taatila V, Suomala J. Default Mode and Executive Networks Areas: Association with the Serial Order in Divergent Thinking. *PLoS One.* (2016) 11:e0162234. doi: 10.1371/journal.pone.0162234
- 37. Beaty RE, Chen Q, Christensen AP, Kenett YN, Silvia PJ, Benedek M, et al. Default network contributions to episodic and semantic processing during divergent creative thinking: A representational similarity analysis. *Neuroimage*. (2020) 209:116499. doi: 10.1016/j.neuroimage.2019.116499
- 38. Miyake A, Friedman NP. The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. *Curr Dir Psychol Sci.* (2012) 21:8–14. doi: 10.1177/0963721411429458
- 39. Yin S, Wang T, Pan W, Liu Y, Chen A. Task-switching Cost and Intrinsic Functional Connectivity in the Human Brain: Toward Understanding Individual Differences in Cognitive Flexibility. *PLoS One.* (2015) 10:e0145826. doi: 10.1371/journal.pone.0145826
- 40. Theriault J, Waytz A, Heiphetz L, Young L. Theory of mind network activity is associated with metaethical judgment: An item analysis. *Neuropsychologia.* (2020) 143:107475. doi: 10.1016/j.neuropsychologia.2020.107475
- 41. Boekel W, Hsieh S. Cross-sectional white matter microstructure differences in age and trait mindfulness. *PLoS ONE*. (2018) 13:e0205718. doi: 10.1371/journal.pone.0205718
- 42. Muda R, Kicia M, Michalak-Wojnowska M, Ginszt M, Filip A, Gawda P, et al. The Dopamine Receptor D4 Gene (DRD4) and Financial Risk-Taking: Stimulating and Instrumental Risk-Taking Propensity and Motivation to Engage in Investment Activity. Frontiers in Behavioral Neuroscience [Internet]. (2018):12. Available from: https://www.frontiersin.org/articles/10.3389/fnbeh.2018.00034
- 43. Smillie LD, Bennett D, Tan NP, Sutcliffe K, Fayn K, Bode S, et al. Does openness/intellect predict sensitivity to the reward value of information? Cognitive. *Affective*, & *Behavioral Neuroscience [Internet]*. (2021) 21:993–1009. doi: 10.3758/s13415-021-00900-1
- 44. Reuter M, Roth S, Holve K, Hennig J. Identification of first candidate genes for creativity: A pilot study. *Brain Research [Internet]*. (2006) 1069:190–7. Available from: https://www.sciencedirect.com/science/article/pii/S0006899305016495
- 45. Rahman MS, Guban P, Wang M, Melas PA, Forsell Y, Lavebratt C. The serotonin transporter promoter variant (5-HTTLPR) and childhood adversity are associated with the personality trait openness to experience. *Psychiatry Res.* (2017) 257:322–6. doi: 10.1016/j.psychres.2017.07.071
- 46. Karg K, Burmeister M, Shedden K, Sen S. The Serotonin Transporter Promoter Variant (5-HTTLPR), Stress, and Depression Meta-analysis Revisited: Evidence of Genetic Moderation. *Arch Gen Psychiatry.* (2011) 68:444–54. doi: 10.1001/archgenpsychiatry.2010.189
- 47. Kalbitzer J, Frokjaer VG, Erritzoe D, Svarer C, Cumming P, Nielsen FA, et al. The personality trait openness is related to cerebral 5-HTT levels. *Neuroimage.* (2009) 45:280–5. doi: 10.1016/j.neuroimage.2008.12.001
- 48. Stenbæk DS, Dam VH, Fisher PM, Hansen N, Hjordt LV, Frokjaer VG. No evidence for a role of the serotonin 4 receptor in five-factor personality traits: A positron emission tomography brain study. *PLoS One*. (2017) 12:e0184403. doi: 10.1371/journal.pone.0184403
- 49. Stenbaek DS, Kristiansen S, Burmester D, Madsen MK, Frokjaer VG, Knudsen GM, et al. Trait Openness and serotonin 2A receptors in healthy volunteers: A positron emission tomography study. *Hum Brain Mapp.* (2019) 40:2117–24. doi: 10.1002/hbm.24511
- 50. Carhart-Harris RL, Bolstridge M, Day CMJ, Rucker J, Watts R, Erritzoe DE, et al. Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. *Psychopharmacology (Berl).* (2018) 235:399–408. doi: 10.1007/s00213-017-4771-x
- 51. Erritzoe D, Roseman L, Nour MM, MacLean K, Kaelen M, Nutt DJ, et al. Effects of psilocybin therapy on personality structure. *Acta Psychiatrica Scandinavica [Internet]*. (2018 [) 138:368–78. doi: 10.1111/acps.12904
- 52. Tagliazucchi E, Carhart-Harris R, Leech R, Nutt D, Chialvo DR. Enhanced repertoire of brain dynamical states during the psychedelic experience. *Hum Brain Mapp.* (2014) 35:5442–56. doi: 10.1002/hbm.22562
- 53. Grimm S, Schubert F, Jaedke M, Gallinat J, Bajbouj M. Prefrontal cortex glutamate and extraversion. Soc Cogn Affect Neurosci. (2012) 7:811–8. doi: 10.1093/scan/nsr056
- 54. Sun J, Shi L, Chen Q, Yang W, Wei D, Zhang J, et al. Openness to experience and psychophysiological interaction patterns during divergent thinking. *Brain Imaging Behav.* (2019) 13:1580–9. doi: 10.1007/s11682-018-9965-2
- 55. Wei D, Yang J, Li W, Wang K, Zhang Q, Qiu J. Increased resting functional connectivity of the medial prefrontal cortex in creativity by means of cognitive stimulation. *Cortex.* (2014) 51:92–102. doi: 10.1016/j.cortex.2013.09.004
- 56. Beaty RE, Kenett YN, Christensen AP, Rosenberg MD, Benedek M, Chen Q, et al. Robust prediction of individual creative ability from brain functional connectivity. *Proc Natl Acad Sci U S A.* (2018) 115:1087–92. doi: 10.1073/pnas.1713532115
- 57. Costa PT Jr, McCrae RR. NEO PI-R professional manual. Odessa, FL: Psychological Assessment Resources, Inc (1992).
- $58.\,\mathrm{Beck}$ AT, Steer RA, Brown GK. Beck depression inventory. New York: Harcourt Brace Jovanovich (1987).
 - 59. Wechsler David. "Wechsler abbreviated scale of intelligence." (1999).

- 60. Raven J, Raven JC, Court JH. Manual for Raven's Progressive Matrices and Vocabulary Scales. In Section 4: The Advanced Progressive Matrices. San Antonio, TX: Harcourt Assessment (1998)
- 61. Lin C, Wang M. *The Creativity Assessment Packet*. Taipei, Taiwan: Psychological Publishing (1994).
- $62.\,Carson$ SH, Peterson JB, DM . Higgins Reliability, validity, and factor structure of the creative achievement questionnaire. Creativity Research Journal. (2005) 17:37–50. doi: 10.1207/s15326934crj 1701_4
- 63. Hocevar Dennis. "The Development of the Creative Behavior Inventory (CBI)." (1979).
- 64. Silvia PJ, Wigert B, Reiter-Palmon R, Kaufman JC. Assessing creativity with self-report scales: A review and empirical evaluation. *Psychology of Aesthetics, Creativity, and the Arts.* (2012) 6:19–34. doi: 10.1037/a0024071
- 65. Donnellan MB, Lucas RE. Age differences in the Big Five across the life span: evidence from two national samples. *Psychol Aging.* (2008) 23:558–66. doi: 10.1037/a0012897
- 66. Hogan MJ, Staff RTBunting BP, Deary IJ, Whalley LJ. Openness to experience and activity engagement facilitate the maintenance of verbal ability in older adults. *Psychol Aging*. (2012) 27:849–54. doi: 10.1037/a0029066
- 67. Giannakopoulos P, Rodriguez C, Montandon ML, Garibotto V, Haller S, Herrmann FR. Less agreeable, better preserved? A PET amyloid and MRI study in a community-based cohort. Neurobiology of Aging [Internet]. (2020) 89:24–31. Available from: https://www.sciencedirect.com/science/article/pii/S0197458020300312
- 68. Stephan Y, Boiché J, Canada B, Terracciano A. Association of personality with physical, social, and mental activities across the lifespan: Findings from US and French samples. *Br J Psychol.* (2014) 105:564–80. doi: 10.1111/bjop.12056
- $69.\ Crowe\ M,\ Andel\ R,\ Pedersen\ NL,\ Fratiglioni\ L,\ Gatz\ M.\ Personality\ and\ risk\ of\ cognitive\ impairment\ 25\ years\ later.\ Psychology\ and\ aging.\ (2006)\ 21:573.$
- 70. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurol.* (2004) 3:343–53. doi: 10.1016/S1474-4422(04)00767-7
- 71. Bonnelle V, Ham TE, Leech R, Kinnunen KM, Mehta MA, Greenwood RJ, et al. Salience network integrity predicts default mode network function after traumatic brain injury. *Proceedings of the National Academy of Sciences [Internet]*. (2012 [) 109:4690–5. doi: 10.1073/pnas.1113455109
- 72. Hafkemeijer A, Möller C, Dopper EG, Jiskoot LC, van den Berg-Huysmans AA, van Swieten JC, et al. A Longitudinal Study on Resting State Functional Connectivity in Behavioral Variant Frontotemporal Dementia and Alzheimer's Disease. *J Alzheimers Dis.* (2017) 55:521–37. doi: 10.3233/JAD-150695
- 73. Cools R, Arnsten A. Neuromodulation of prefrontal cortex cognitive function in primates: the powerful roles of monoamines and acetylcholine. *Neuropsychopharmacology.* (2021) 47:1–20. doi: 10.1038/s41386-021-01100-8
- 74. Agosta F, Scola E, Canu E, Marcone A, Magnani G, Sarro L, et al. White matter damage in frontotemporal lobar degeneration spectrum. *Cereb Cortex.* (2012) 22:2705–14. doi: 10.1093/cercor/bhr288
- 75. Kudlicka A, Clare L, Hindle JV. Executive functions in Parkinson's disease: systematic review and meta-analysis. *Mov Disord.* (2011) 26:2305–15. doi: 10.1002/mds.23868
- 76. Santangelo G, Piscopo F, Barone P, Vitale C. Personality in Parkinson's disease: Clinical, behavioural and cognitive correlates. *J Neurol Sci.* (2017) 374:17–25. doi: 10.1016/j.jns.2017.01.013
- 77. Terracciano A, Sutin AR, An Y, O'Brien RJ, Ferrucci L, Zonderman AB, et al. Personality and risk of Alzheimer's disease: new data and meta-analysis. *Alzheimers Dement.* (2014) 10:179–86. doi: 10.1016/j.jalz.2013.03.002
- 78. Chapman BP, Huang A, Peters K, Horner E, Manly J, Bennett DA, et al. Association Between High School Personality Phenotype and Dementia 54 Years Later in Results From a National US Sample. *JAMA Psychiatry.* (2020) 77:148–54. doi: 10.1001/jamapsychiatry.2019.3120
- 79. Ihle A, Zuber S, Gouveia ÉR, Gouveia BR, Mella N, Desrichard O, et al. Cognitive Reserve Mediates the Relation between Openness to Experience and Smaller Decline in Executive Functioning. *Dement Geriatr Cogn Disord.* (2019) 48:39–44. doi: 10.1159/000501822
- $80.\,Williams$ S. More than Education: Openness to Experience Contributes to Cognitive Reserve in Older Adulthood. Journal of Aging. Science.~(2013):01.

- 81. Giannakopoulos P, Rodriguez C, Montandon ML, Garibotto V, Haller S, Herrmann FR. Less agreeable, better preserved? A PET amyloid and MRI study in a community-based cohort. *Neurobiol Aging*. (2020) 89:24–31. doi: 10.1016/j.neurobiolaging.2020.02.004
- 82. Terracciano A, Bilgel M, Aschwanden D, Luchetti M, Stephan Y, Moghekar AR, et al. Personality Associations With Amyloid and Tau: Results From the Baltimore Longitudinal Study of Aging and Meta-analysis. *Biol Psychiatry.* (2022) 91:359–69. doi: 10.1016/j.biopsych.2021.08.021
- 83. Tautvydaitė D, Kukreja D, Antonietti JP, Henry H, von Gunten A, Popp J. Interaction between personality traits and cerebrospinal fluid biomarkers of Alzheimer's disease pathology modulates cognitive performance. *Alzheimers Res Ther.* (2017) 9:6. doi: 10.1186/s13195-017-0235-0
- 84. Santangelo G, Garramone F, Baiano C, D'Iorio A, Piscopo F, Raimo S, et al. Personality and Parkinson's disease: A meta-analysis. *Parkinsonism Relat Disord.* (2018) 49:67–74. doi: 10.1016/j.parkreldis.2018.01.013
- 85. Rankin KP, Kramer JH, Mychack P, Miller BL. Double dissociation of social functioning in frontotemporal dementia. *Neurology*. (2003) 60:266–71. doi: 10.1212/01. wnl.0000041497.07694.d2
- 86. Kumfor F, Irish M, Hodges JR, Piguet O. The orbitofrontal cortex is involved in emotional enhancement of memory: evidence from the dementias. *Brain.* (2013) 136:2992–3003. doi: 10.1093/brain/awt185
- 87. Rankin KP, Liu AA, Howard S, Slama H, Hou CE, Shuster K, et al. A case-controlled study of altered visual art production in Alzheimer's and FTLD. *Cogn Behav Neurol.* (2007) 20:48–61. doi: 10.1097/WNN.0b013e31803141dd
- 88. Hornberger M, Geng J, Hodges JR. Convergent grey and white matter evidence of orbitofrontal cortex changes related to disinhibition in behavioural variant frontotemporal dementia. *Brain [Internet]*. (2011) 134:2502–12. doi: 10.1093/brain/awr173
- 89. Seeley WW, Crawford RK, Zhou J, Miller BL, Greicius MD. Neurodegenerative diseases target large-scale human brain networks. *Neuron.* (2009) 62:42–52. doi: 10.1016/j.neuron.2009.03.024
- 90. Younes K, Borghesani V, Montembeault M, Spina S, Mandelli ML, Welch AE, et al. Right temporal degeneration and socioemotional semantics: semantic behavioural variant frontotemporal dementia. *Brain*. (2022) 145:4080–96. doi: 10.1093/brain/ awac217
- 91. Seeley WW, Bauer AM, Miller BL, Gorno-Tempini ML, Kramer JH, Weiner M, et al. The natural history of temporal variant frontotemporal dementia. *Neurology.* (2005) 64:1384–90. doi: 10.1212/01.WNL.0000158425.46019.5C
- 92. Josephs KA, Whitwell JL, Knopman DS, Boeve BF, Vemuri P, Senjem ML, et al. Two distinct subtypes of right temporal variant frontotemporal dementia. *Neurology.* (2009) 73:1443–50. doi: 10.1212/WNL.0b013e3181bf9945
- 93. Barrash J, Tranel D, Anderson SW. Acquired personality disturbances associated with bilateral damage to the ventromedial prefrontal region. *Dev Neuropsychol.* (2000) 18:355–81. doi: 10.1207/S1532694205Barrash
- 94. Rankin KP, Rosen HJ, Kramer JH, Schauer GF, Weiner MW, Schuff N, et al. Right and left medial orbitofrontal volumes show an opposite relationship to agreeableness in FTD. *Dement Geriatr Cogn Disord.* (2004) 17:328–32. doi: 10.1159/000077165
- 95. Zhou J, Gennatas ED, Kramer JH, Miller BL, Seeley WW. Predicting regional neurodegeneration from the healthy brain functional connectome. *Neuron.* (2012) 73:1216–27. doi: 10.1016/j.neuron.2012.03.004
- 96. Miller BL, Hou CE. Portraits of Artists: Emergence of Visual Creativity in Dementia. *Archives of Neurology [Internet]*. (2004) 61:842–4. doi: 10.1001/archneur.61.6.842
- 97. Friedberg A, Pasquini L, Diggs R, Glaubitz EA, Lopez L, Illán-Gala I, et al. Prevalence, Timing, and Network Localization of Emergent Visual Creativity in Frontotemporal Dementia. *JAMA Neurology [Internet]*. (2023). doi: 10.1001/jamaneurol.2023.0001
- 98. Erkkinen MG, Zúñiga RG, Pardo CC, Miller BL, Miller ZA. Artistic Renaissance in Frontotemporal Dementia. *JAMA*. (2018) 319:1304–6. doi: 10.1001/jama.2017.19501
- 99. Miller BL, Seeley WW, Mychack P, Rosen HJ, Mena I, Boone K. Neuroanatomy of the self. *Neurology [Internet]*. (2001) 57:817. Available from: http://n.neurology.org/content/57/5/817.abstract
- 100. Rosen HJ, Perry RJ, Murphy J, Kramer JH, Mychack P, Schuff N, et al. Emotion comprehension in the temporal variant of frontotemporal dementia. *Brain*. (2002) 125:2286–95. doi: 10.1093/brain/awf225