<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6144503/>

Angiotensin IV suppresses inflammation in the brains of rats with chronic cerebral hypoperfusion

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3814522/>

Playing piano makes one happier and smarter

"Professional musicians have been found to have greater than average gray matter in motor, auditory, and visuospatial areas, differences in white matter architecture, stronger asymmetry of the planum temporale, and increased corpus callosum"

"Furthermore, it has been demonstrated that there is a strong correlation between high musical activity during the lifespan and preservation of non-verbal memory, naming, and executive function"

"the most compelling evidence of the effects of musical training is from longitudinal studies on child populations. Schellenberg (2004) found that children who received 36-weeks musical lessons (standard keyboard or Kodálay) showed a small but significant increase in IQ compared to children who took drama lessons or no lessons at all. Furthermore, it has been shown that 6-year-old children who received 15 months private keyboard lessons showed structural brain changes that correlated with improvements in musically relevant auditory and motor skills when compared to a control group that did not received such instruction"

"Finally, a series of follow-up studies comparing 8-year-old children who received either music or painting lessons for several months, found that music training has transfer effects to linguistic abilities evidenced by improvements in behavioral measures and electrophysiological responses, while painting lessons do not"

"even short-term musical training in adults can induce cortical plasticity."

"Some studies suggest that musical training in the older stages of life can mitigate effects of the aging brain (for a review see Wan and Schlaug, 2010). Verghese et al. (2003), in a follow-up study of elderly people, observed that those individuals who played a musical instrument were less likely to suffer dementia than participants involved in other type of leisure activities like reading, writing, or doing crossword puzzles. Surprisingly, in this study physical activity was not associated with a lower risk of suffering dementia"

"6 months of individualized piano lessons in older adults improved executive functioning and working memory (Bugos et al., 2007), although not all cognitive benefits were maintained in a 3-month follow-up"

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7704181/>

"Our findings indicate that brief mindfulness meditation induces gray matter plasticity, suggesting that structural changes in ventral PCC—a key hub associated with self-awareness, emotion, cognition, and aging—may have important implications for protecting against mood-related disorders and aging-related cognitive declines."

<https://www.frontiersin.org/articles/10.3389/fpsyg.2014.01551/full>

<https://news.harvard.edu/gazette/story/2011/01/eight-weeks-to-a-better-brain/>

"Participating in an eight-week mindfulness meditation program appears to make measurable changes in brain regions associated with memory, sense of self, empathy, and stress. In a study that will appear in the Jan. 30 issue of Psychiatry Research: Neuroimaging, a team led by Harvard-affiliated researchers at Massachusetts General Hospital (MGH) reported the results of their study, the first to document meditation-produced changes over time in the brain’s gray matter."

"Our RCT results demonstrate that 10 h of IBMT induced gray matter changes in ventral PCC/ISC—a brain hub associated with cognition, emotion, and self-related processes (e.g., self-awareness). Moreover, temperamental traits reflecting negative affect predicted the extent of training-induced gray matter volumetric increases in ventral PCC/ISC, suggesting a predisposing role of individual differences in influencing training-induced gray matter plasticity. These findings may have important implications for understanding the pathophysiology of—and monitoring—therapeutic interventions in mood-related disorders and aging-related cognitive decline that often manifest functional and structural abnormalities within these brain regions"

"hippocampus, a structure critical for memory, has also been shown to increase in volume in long-term meditators [1, 5]. Conversely, reduction in volume was often detected in the amygdala in meditation studies [44, 46], suggesting that this subcortical structure associated with emotion and stress may manifest a different trend of structural plasticity, and may underlie the behavioral reduction of stress reactivity commonly observed in meditators."

<https://www.sciencedirect.com/science/article/pii/S1871403X21001150>

"Insertion of IGB lead to 8.9% and 12.3% weight reduction over the first three months and over the entire treatment, respectively. Over the entire treatment, total gray matter volume increased by 2.0% (p = 0.009). These changes were mostly pronounced in the left precuneus and in the right frontal pole (>1.9%, p < 0.009). The increases in cortical volume in the right hemisphere and the left posterior cingulate cortical thickness over the entire treatment were significantly related to decreases in myo-inositol ratios measured over the first three months of the treatment"

"IGB treatment lead to brain structural improvements consistent with earlier studies of bariatric patients without co-morbid conditions. Our results also pointed to improvements in brain regions, where atrophy in other studies was related to type 2 diabetes and hypertension. The correlations point to neuroinflammation as one of the potential processes behind brain volume reductions in patients with morbid obesity"

<https://www.sciencedirect.com/science/article/pii/S0197458014003492>

"We conclude that higher cardiorespiratory fitness levels are routinely associated with greater gray matter volume in the prefrontal cortex and hippocampus and less consistently in other regions. We also conclude that physical activity is associated with greater gray matter volume in the same regions that are associated with cardiorespiratory fitness including the prefrontal cortex and hippocampus."

<https://www.pnas.org/doi/10.1073/pnas.1103217108>

Learning new colors grey matter

<https://www.awakeningfromalzheimers.com/the-wonder-drug-of-neurology/>

“it would take 10 million times as much BDNF to get as much new synapse formation as Dihexa.”

She calls Dihexa “an extraordinary peptide that is able to recover brain function,” for people with traumatic brain injuries and dementia.

"At the Biohacker Summit held in Helsinki, Finland in November, he said Dihexa is “amazing for learning and memory” and is “really good” for learning to play a new instrument or learning a foreign language faster."

<https://www.nature.com/articles/s41467-018-04268-8>

"research has demonstrated that individuals with higher intelligence are more likely to have larger gray matter volume in brain areas predominantly located in parieto-frontal regions."

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948283/>

"This study demonstrates that recovery of verbal memory and focused attention improved significantly and substantially in the group of patients who listened to their favourite music on a daily basis compared with patients who listened to audio books or received no listening material."

"musicians showed no or a smaller decrease in grey matter density in the frontal cortex compared with non-musicians with increasing age."

<https://www.sciencedirect.com/science/article/pii/S1053811921005814>

"It is commonly believed that white matter is not involved in adult neuroplasticity; however, studies in rodents have shown experience-dependent changes in oligodendrocyte differentiation (McKenzie et al., 2014; Simon et al., 2011), myelination (Chorghay et al., 2018; Kato et al., 2020), and axonal diameter (Bobinski et al., 2011), which correlated with improved motor and cognitive performance"

"aerobic walking training resulted in an increase in the white matter T1w/T2w signal, relative to an active control condition which included flexibility, strength, and balance exercises. Thus, our findings are in alignment with the previous cross-sectional and intervention studies showing a positive relationship between aerobic exercise, gray matter structure, and functional activity"

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7247733/>

"Possibly, this suggests that larger GM volume in these clusters may be protective against sleepiness in older individuals"

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677584/>

"documented in detail, including psychodynamic formulations, a female musical savant whom he followed for many years. Treffert (2006a) described a blind, autistic musical savant who, along with her musical ability, demonstrated very precise spatial location abilities and precise time-keeping skills without access to a clock face or other time instruments."

"suggests that savant skills may result from the formation of exceptional

neural structures during prenatal brain development however the causes of savant skills

remain unclear and controversial. There is mounting evidence for a genetic link with family

members displaying similar interests, talents and abilities (Hermelin & O’Connor, 1990b;

Young & Nettlebeck, 1995)."

<https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-020-02722-w>

"Synesthesia is a sensory phenomenon where certain domain-specific stimuli trigger additional sensations of e.g. color or texture. The condition occurs in about 4% of the general population, but is overrepresented in individuals with Autism Spectrum Disorder (ASD), where it might also be associated with the presence of prodigious talents."

"this case study endorses the notion of a link between synesthesia, prodigious talent and autism, adding to the currently still sparse literature in this field. It provides new insights into the possible manifestations of synesthesia in individuals with ASD and its potential contribution to prodigious talents in people with an otherwise unexceptional cognitive profile. Additionally, this case impressively illustrates how synesthesia can be a key element not only of sensory perception but also social and emotional processing and contributes to existing evidence of increased brain connectivity in association with synesthesia."

**I was super good at guessing times on noopept; why?**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6946735/>

"A recent finding related to sensory atypicalities in autism is a frequent co-occurrence of ASD with synaesthesia, another neurodevelopmental condition. Synaesthesia, which can be translated from Greek as ‘joined perception’, is characterized by altered perceptual experiences: perceiving an inducing stimulus elicits an unusual concurrent sensation in the same or a different modality, e.g. letters automatically evoke a colour. Whereas the general prevalence of synaesthesia only lies around ~ 4% (Simner et al. 2006), approximately 20% of people with ASD have synaesthesia"

"Over the last decades, an increasing amount of evidence has been collected that suggests ASD to fall on a continuum, ranging from a low to high degree of autistic traits (Baron-Cohen et al. 2001; De Groot and Van Strien 2017; Hoekstra et al. 2008). The quantitative nature of ASD has been termed the broader autism phenotype (BAP)."

"One aspect of sensory perception is sensory sensitivity, which is frequently atypical in individuals with ASD, e.g. characterized by hyper- and/or hyposensitivity to sounds or touch (for a review, see Schauder and Bennetto 2016). More recently, similar patterns of increased and decreased sensory sensitivity (measured with the Glasgow Sensory Questionnaire) were found in both ASD and synaesthesia (Ward et al. 2017, 2018; Van Leeuwen et al. 2019), revealing particularly strong hyper- and hyposensitivity to auditory stimulation in both conditions."

"In line with the findings for autism, synaesthetes have scored higher than controls on the Attention-to-detail subscale of the Autism Spectrum Quotient (AQ) (Mealor et al. 2016; Van Leeuwen et al. 2019; Ward et al. 2017, 2018), a self-report questionnaire on autistic traits. This finding suggests a shared bias in local visual perception between ASD and synaesthesia. Ward et al. (2018) also showed that synaesthetes outperformed controls on two tests requiring attention to detail, extending the perceptual commonalities between ASD and synaesthesia from the phenomenal (self-report) level to functioning at cognitive tasks."

"when individuals with ASD are presented with hierarchical stimuli (Navon 1977) they tend to attend to the local rather than the global level of these stimuli (Koldewyn et al. 2013; Muth et al. 2014)."

"studies into ASD and synaesthesia have found neural similarities related to visual perception, such as enhanced sensitivity of the parvocellular visual pathway (sensitive to fine detail and high contrast)"

"In the limited dot lifetime condition, participants are forced to use the global strategy, as the dot lifetime is too short to track single dots. Because of the hypothesized local bias, we expect a higher degree of autistic traits and synaesthesia to be related to impaired performance in this condition."

"We investigated the relation between the degree of autistic traits (as measured with the Autism Quotient) and the degree of grapheme-colour synaesthesia (as measured with a consistency test) in neurotypicals, and whether this relation is accompanied by a shared bias towards local (detail-focussed) visual perception. In line with our first hypothesis, a positive relation exists between the degree of autistic traits (AQ-total scores) and the degree of synaesthesia. In addition, and supporting our second hypothesis, a relation was found between the AQ-attention to detail subscores and a bias towards local visual perception, as indicated by performance on the Embedded Figures Task (EFT) and (to a lesser extent) the visual illusions task."

<https://www.sciencedirect.com/science/article/pii/S001094522100321X>

"Our study has provided insight into the perceptual experiences and abilities inherent to synaesthesia and ASD, as well as into their relationship. We found a positive relation between the degree of synaesthesia and autistic traits, one of the first demonstrations of this relation in a neurotypical sample. Furthermore, we found a relation between the degree of autistic traits and a bias towards local visual perception"

This is the first twin study on the association between synesthesia and autism-related perceptual features and traits. The results suggest that investigating these associations within-twin pairs, implicitly adjusting for potential confounding factors shared by twins, is more sensitive than doing so in non-related individuals. Consistent with previous findings, the results suggest an association between the degree of grapheme-color synesthesia and autism-related perceptual features, while utilizing a different measure for sensory sensitivity. The novel finding of enhanced fragmented picture integration in twins with a higher degree of grapheme-color synesthesia challenges the view of a generally more detail-focused attentional style in synesthesia and might be related to enhanced memory or mental imagery in more synesthetic individuals."

<https://www.google.com/url?sa=t&source=web&rct=j&url=https://lirias.kuleuven.be/retrieve/631784&ved=2ahUKEwibnJzSm4X6AhWtBUQIHZcnB08QFnoECAkQAQ&usg=AOvVaw1GsnCiJpZYXheXWIgK-mlj>

"Developmental and epileptic encephalopathies (DEEs) are complex conditions characterized primarily by seizures associated with neurodevelopmental and motor deficits. Recent evidence

supports sigma-1 receptor modulation in both neuroprotection and antiseizure activity, suggesting

that sigma-1 receptors may play a role in the pathogenesis of DEEs, and that targeting this receptor"

"In conclusion, Sigma1R function (or dysfunction) is linked to multiple facets of the

DEE phenotype, including both seizures and non-seizure comorbidities. In this context,

it is notable that fenfluramine—with profound antiseizure activities in two DEEs (Dravet

and Lennox-Gastaut syndromes)—was recently discovered to be a positive modulator of

Sigma1R activity, in addition to its known 5-HT activity. The empirical evidence reviewed

in this report suggests a model whereby fenfluramine restores the homeostatic balance

between inhibitory GABAergic and excitatory glutamatergic activity to dampen seizure

activity in Dravet syndrome and other DEEs (Figure 1). Data from zebrafish models suggest

that fenfluramine restores dendritic arborization of GABAergic neurons. At glutamatergic

synapses, fenfluramine appears to coordinate with endogenous ligands (e.g., neuroactive

steroids) to positively modulate Sigma1R-mediated interaction with the NMDAR, thereby

dampening calcium flux and reducing seizure activity at glutamatergic synapses. Further,

coordinated interaction with Sigma1R and agonism at 5HT1D, 5HT2A, and 5HT2C receptors

are hypothesized to modulate calcium influx into the ER via a Gq/IP3R-mediated mechanism (Figure 2). Control of calcium flux via Sigma1R-mediated mechanisms further helps

to restore the balance between inhibitory and excitatory input to decrease seizure activity.

Further research into the role of Sigma1R in DEE pathology is warranted, including its role

in seizure control and in non-seizure outcomes associated with DEE"

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7819932/>

"Mutations in synaptic genes and alterations of mitochondrial functions are considered important underlying pathogenic factors"

"Autism spectrum disorder (ASD) is a neurodevelopmental condition that starts in childhood and prevails across the lifespan, symptoms are variable, and a substantial increase in ASD diagnosis has been reported during the last 40 years [1]. A significant part of ASD cases is associated with mutations in synaptic proteins, suggesting an impairment of synaptic transmission as a primary underlying cause [2–7]. Synaptic activity is an energetically expensive process that consumes a large proportion of the adenosine triphosphate (ATP) generated in neurons, which is mainly produced by mitochondria through oxidative phosphorylation (OXPHOS) [8]."

"Besides their role as energy providers, mitochondria also act as calcium (Ca2+) buffers that shape the synaptic response"

"Besides their role as energy providers, mitochondria also act as calcium (Ca2+) buffers that shape the synaptic response [13]. Hence, their presence at the synapse serves not only to produce ATP but also to control local Ca2+ concentrations ([Ca2+]) and neurotransmitter release, which is essentially triggered by a sudden increase in Ca2+ concentration."

"Other tethering complexes are formed by proteins like the protein tyrosine phosphatase-interacting protein 51 (PTPIP51), the vesicle-associated membrane protein-associated protein B (VAPB), and the B cell receptor–associated protein (BAP31), which are also associated with Ca2+ handling [26]. Interestingly, mutations in VAPB and S1R are related to neurodegenerative diseases [27,"

"Several neurodevelopmental disorders are characterized by a combination of metabolic disease and synaptic disturbances [92, 93]. SHANK proteins, for example, predominantly serve as adaptor and scaffolding proteins in the PSD and connect ionotropic and metabotropic glutamate receptors (mGluR) with the actin cytoskeleton [94]; their mutations are implicated in multiple neuropsychiatric disorders, including ASD, schizophrenia, and intellectual disability to name the most frequently occurring"

"was also reported that mitochondrial dysfunction could be recovered after treatment with the selective agonist LP-211, which stimulates the brain serotonin receptor 7 (5-HT7R)."

"it is unclear if the mitochondrial defects found in these disease models can be solely attributed to increased respiration and if these alterations are the consequence of redox imbalances. Similar results were obtained in a previous study performed in isolated mitochondria from whole brains of Mecp2-KO mice that also found significantly higher respiration rates than WT, and the mitochondrial ubiquinol-cytochrome c reductase core protein 1 (Uqcrc1) gene was upregulated [145]. To summarize, there is considerable evidence linking RS and mitochondrial dysfunction in patients and animal models of the disease [146]. Interventions targeting mitochondria might be beneficial in the treatment of RS."

"Similar results were obtained in a previous study performed in isolated mitochondria from whole brains of Mecp2-KO mice that also found significantly higher respiration rates than WT, and **the mitochondrial ubiquinol-cytochrome c reductase** core protein 1 (Uqcrc1) gene was upregulated [145]"

"The gene encoding ubiquitin-protein ligase E3A (UBE3A) is localized to the 15q11-15q13 chromosome in humans. UBE3A deficiency is responsible for Angelman syndrome (AS), a severe neurological condition characterized by cognitive impairment and developmental delay. Patients with AS often present with ASD features, although there is an unresolved controversy about considering AS and ASD independent from each other [152]. Increased expression of the Ube3a gene in mice produced autistic-like behaviors [153]. Additionally, reduced function of complex III in patients with the 15q11-q13 duplication syndrome has been documented [154]. The role of mitochondria has been studied mainly in AS mouse models, like the heterozygous mice Ube3am-\p+ [155], in which Ube3a was found in close proximity to the outer mitochondrial membrane [156]. Mitochondrial morphological changes in the CA1 hippocampal region were found, like smaller mitochondria and disturbances in mitochondrial cristae compared to WT littermates [157]. Mitochondria were isolated from the hippocampus, cortex, and cerebellum, and the activities of the different components of the electron transport chain (ETC) were tested [158]. A significantly reduced activity of complex III was found in the cortex and hippocampus. **Electron flow was recovered by administering a Coenzyme Q10 (CoQ10) analog, increasing the protein expression levels of complexes III and IV in neurons from hippocampal regions** CA1, CA2, and CA3 and the cerebellum. Nonetheless, oxidative stress was decreased only in the hippocampus when measuring the GSH and glutathione disulfide (GSSG) ratio,"

“To summarize, there is accumulating evidence showing mitochondrial dysfunction in different *Fmr1* mutant models, including Drosophila [[116](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7819932/#CR116)]. Although some of the findings point to an indirect relationship, others suggest that altered translation of mitochondrial proteins at the synapse is a possible mechanism behind disorders like FXS. More studies are necessary to understand how mitochondria contribute to the development of the FXS or if impairments in mitochondrial function are just an epiphenomenon.”

“The DiGeorge syndrome, also known as velocardiofacial or 22q11.2 deletion syndrome (22q11.2DS), is the consequence of a hemizygous microdeletion (1.5–3 Mb) on chromosome 22, with an incidence of 1 in 4000 [[117](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7819932/#CR117)]. The syndrome often presents with different neuropsychiatric symptoms [[118](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7819932/#CR118)], including schizophrenia [[119](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7819932/#CR119)]. Additionally, individuals with 22q11.2DS manifest with attention-deficit hyperactive disorder (ADHD), ASD, anxiety, depressive, and bipolar disorders”

<https://www.sciencedirect.com/science/article/pii/S1071909120300401>

“A suspicion of the mitochondrion's involvement in ASD can be traced back to 1985 when [lactic acidosis](https://www.sciencedirect.com/topics/medicine-and-dentistry/lactic-acidosis) was noted in a subset of children with ASD. A large population-based study in 2007 confirmed this notion and found that a subset of children with ASD (∼4%) could be diagnosed with a definite [mitochondrial disease](https://www.sciencedirect.com/topics/medicine-and-dentistry/disorders-of-mitochondrial-functions). Further studies suggested that children with ASD and mitochondrial disease may have certain characteristics such as fatigability, [gastrointestinal disorders](https://www.sciencedirect.com/topics/medicine-and-dentistry/gastrointestinal-disease), unusual types of neurodevelopmental regression, seizures/epilepsy, and motor delay. Further research examining biomarkers of mitochondrial dysfunction and [electron transport chain](https://www.sciencedirect.com/topics/medicine-and-dentistry/respiratory-chain) activity suggest that abnormalities of mitochondrial function could affect a much higher number of children with ASD, perhaps up to 80%. Recent research has identified a type of dysfunction of mitochondria in which the activity of the electron transport chain is significantly increased. This novel type of mitochondrial dysfunction may be associated with environmental exposures and neurodevelopmental regression. Several treatments that target mitochondria appear to have evidence for use in children with ASD, including [cofactors](https://www.sciencedirect.com/topics/neuroscience/cofactor) such as L-Carnitine and the [ketogenic diet](https://www.sciencedirect.com/topics/medicine-and-dentistry/ketogenic-diet). “

“in 1985 Mary Coleman at Georgetown University found that 5% of children with ASD demonstrated [lactic acidosis](https://www.sciencedirect.com/topics/medicine-and-dentistry/lactic-acidosis) and proposed that they may suffer from a defect in [carbohydrate metabolism](https://www.sciencedirect.com/topics/medicine-and-dentistry/carbohydrate-metabolism) linked to the [pyruvate dehydrogenase complex](https://www.sciencedirect.com/topics/neuroscience/pyruvate-dehydrogenase-complex).[13](https://www.sciencedirect.com/science/article/pii/S1071909120300401#bib0013) Perhaps the strongest evidence supporting the notion that mitochondrial disease is associated with ASD was a population-based study of Portugal and the Azores which screened over 300,000 school-age children for ASD and investigated co-morbid medical conditions.[14](https://www.sciencedirect.com/science/article/pii/S1071909120300401#bib0014) Lactic acidosis was found in 20% of the cases of ASD that underwent medical investigation with 46% of the individuals that underwent further investigation for lactic acidosis being diagnosed with a definite mitochondrial [respiratory chain](https://www.sciencedirect.com/topics/medicine-and-dentistry/respiratory-chain) disorder, resulting in a prevalence of 4.2% of the overall ASD sample having a diagnosis of a definite mitochondrial respiratory chain disorder.”  
  
“Additional case studies and series continued to document the association with mitochondrial disease and ASD with one particularly large case series pointing out that children with ASD and mitochondrial disease had high rates of fatigability, [gastrointestinal disorders](https://www.sciencedirect.com/topics/medicine-and-dentistry/gastrointestinal-disease), and unusual types of neurodevelopmental regression (NDR) including multiple regressions or regression later than commonly associated with ASD”

<https://pubmed.ncbi.nlm.nih.gov/25704836/>

Synaesthesia in twins

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3222625/>

"proposed that synesthesia results from an excess of neural connections between associated modalities, possibly due to decreased neural pruning between (typically adjacent) regions that are interconnected in the fetus. Consistent with this suggestion, a number of studies have demonstrated anatomical differences in the inferior temporal lobe near regions related to grapheme and color processing in synesthetes, including increased fractional anisotropy (reflecting increased white matter or coherence of white matter) [8],[9] and increased gray matter volume"

<https://academic.oup.com/brain/article/132/1/65/290177>

"one model of (grapheme-colour) synaesthesia proposes that over-activity in parietal regions, where the binding of different sensory information into coherent representations physiologically occurs, leads to stronger than normal binding of, e.g. colours and graphemes, resulting in the additional abnormal synaesthestic experiences"

<https://www.jneurosci.org/content/30/18/6205>

"Specifically, the synesthetic color can be experienced “in the mind” (associator synesthetes) or “in the outside world” (projector synesthetes). Gray matter structure and functioning (imaged using voxel-based morphometry and functional magnetic resonance imaging, respectively) were examined in grapheme–color synesthetes (N = 42, 16 projectors and 26 associators) and nonsynesthetes. Results indicated partly shared mechanisms for all grapheme–color synesthetes, particularly in posterior superior parietal lobe"

"The role of the parietal lobe in synesthesia has been related to its function in cross-sensory integration or “binding,” multimodal associations, and multimodal integratory attention"

"Increased GM in projector synesthetes was found located in the visual cortex (Fig. 3). This region of increased GM is located at the most anterior GM near intracalcarine sulcus in the left hemisphere"

"A third region of increased GM in projectors compared with associator synesthetes is in the left precentral gyrus. This region is functionally described as the premotor and supplementary motor cortex. Increased GM for projectors compared with associators was also found in superior precuneus cortex."

"Overall, the areas can be summarized as brain regions involved in sensory experiences (auditory in Heschl's gyrus, visual in calcarine sulcus, secondary somatosensory in parietal operculum, and possibly taste in insula) and planning action (precentral gyrus)."

"Projectors, compared with associators, show increased GM around right superior frontal sulcus (superior frontal gyrus, extending to middle frontal gyrus). Increased GM in the left hemisphere was located mostly in medial frontal gyrus. Both regions occupy a large anterior–posterior region of the superior part of the frontal lobe."

"The covariate analysis found six regions of increased gray matter in associator synesthetes compared with projector synesthetes. Three of these regions are located in the hippocampal area. The first region overlaps strongly with the associator region found in the contrast analysis, reported previously. This region is located in the right hippocampus, possibly extending into the right thalamus. Increased GM was also found in the anterior part of the right hippocampus, extending into right amygdala. The third region is located in the left hippocampus, parahippocampal gyrus, and temporal fusiform gyrus and extends into the posterior part of the thalamus (Fig. 4). This region in left hemisphere is located bilaterally from the two regions in the right hemisphere."

"Next to these regions in the hippocampal region, we found increased gray matter in right cerebellum, extending into the occipital lobe and bilaterally in the angular gyrus. The left region is located in angular gyrus, extending into superior temporal lobe. The right region is located in angular gyrus and the intraparietal sulcus, extending into superior parietal lobe (Fig. 4).

The regions related to associator synesthesia were found most prominently in hippocampus and in the angular gyrus. The hippocampus is mostly known for its function in memory and spatial memory. Functions ascribed to the angular gyrus are making an association between different types of information [e.g., in use of language (Geschwind, 1972)], a “core quantity system” (Dehaene et al., 2003), and the use of metaphors (Ramachandran, 2004)."

"These results indicate that multimodal brain areas, most distinctively in parietal cortex, are activated during synesthesia, for both projector and associator subtype"

<https://pubmed.ncbi.nlm.nih.gov/11798382/>

"The aim of this study was to identify changes in brain activity associated with the increase in working memory (WM) capacity that occurs during childhood and early adulthood. Functional MRI (fMRI) was used to measure brain activity in subjects between 9 and 18 years of age while they performed a visuospatial WM task and a baseline task. During performance of the WM task, the older children showed higher activation of cortex in the superior frontal and intraparietal cortex than the younger children did. A second analysis found that WM capacity was significantly correlated with brain activity in the same regions. These frontal and parietal areas are known to be involved in the control of attention and spatial WM. The development of the functionality in these areas may play an important role in cognitive development during childhood."

<https://www.sciencedirect.com/science/article/pii/S0301008217300618>

"The neural substrates of apathy have been suggested to lie in circuits linking the prefrontal cortex to subcortical structures (Bonelli and Cummings, 2007; Brown and Pluck, 2000; Levy and Dubois, 2006; Marin, 1990; Starkstein, 2000; Stuss et al., 2000; van Reekum et al., 2005). Indeed, studies in various disorders have implicated the dopaminergic system (Czernecki et al., 2008; Tanaka et al., 2003; Thobois et al., 2010), cholinergic system (Drijgers et al., 2009), and noradrenergic system (Barnhart et al., 2004) in apathy. The circuits linking these systems particularly to the striatum and prefrontal cortex are considered to be the basis of disorders of motivation. These disorders include severe behavioral impairment seen in akinetic mutism where patients are unresponsive to external commands, lack motor initiative, and are indifferent to internal states of pain or thirst (Mega and Cohenour, 1997). This condition as well as a similar but less severe condition, termed abulia, are closely associated with lesions in the anterior cingulate cortex, ventral or limbic striatum (consisting of the ventral caudate, ventral putamen, nucleus accumbens, and olfactory tubercle), the ventral global pallidus, and medial thalamus (Mega and Cohenour, 1997). On the basis of these studies, cortico-subcortical loops from the anterior cingulate cortex to the thalamus and striatum, and brainstem nuclei have been proposed to underlie motivational disorders in general (Bonelli and Cummings, 2007). The emphasis on frontostriatal circuits is easy to understand, as it is not only by inference of well-described functions attributed to these circuits that correspond with deficits expressed in apathy (Hazy et al., 2007; Miller and Cohen, 2001), but there is also empirical evidence for their association in apathy"

<https://pubmed.ncbi.nlm.nih.gov/15483594/>

"Humans have a unique ability to learn more than one language--a skill that is thought to be mediated by functional (rather than structural) plastic changes in the brain. **Here we show that learning a second language increases the density of grey matter in the left inferior parietal cortex** and that the degree of structural reorganization in this region is modulated by the proficiency attained and the age at acquisition. This relation between grey-matter density and performance may represent a general principle of brain organization."

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5543091/>

"Univariate voxel-based morphometry analyses revealed that regional gray matter volume was lower in the ASD than in the control group in several brain regions, including the right inferior occipital gyrus, left fusiform gyrus, right middle temporal gyrus, bilateral amygdala, right inferior frontal gyrus, right orbitofrontal cortex, and left dorsomedial prefrontal cortex."

<https://pubmed.ncbi.nlm.nih.gov/28181668/>

"Histopathological assessment of stroke brains from NSI-189-treated animals revealed significant increments in neurite outgrowth as evidenced by MAP2 immunoreactivity that was prominently detected in the hippocampus and partially in the cortex. These results suggest NSI-189 actively stimulated remodeling of the stroke brain."

8 region, which is a pro-cognitive signal.

Researchers concluded that these electrophysiological changes are consistent with the neurogenic hypothesis of the drug mechanism, which involves long-term structural changes in the hippocampus"

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Background

Voxel-based morphometry (VBM) studies in autism spectrum disorder (autism) have yielded diverging results. This might partly be attributed to structural alterations being associating with the combined influence of several regions rather than with a single region. Further, these structural covariation differences may relate to continuous measures of autism rather than with categorical case–control contrasts. The current study aimed to identify structural covariation alterations in autism, and assessed canonical correlations between brain covariation patterns and core autism symptoms.

Methods

We studied 347 individuals with autism and 252 typically developing individuals, aged between 6 and 30 years, who have been deeply phenotyped in the Longitudinal European Autism Project. All participants’ VBM maps were decomposed into spatially independent components using independent component analysis. A generalized linear model (GLM) was used to examine case–control differences. Next, canonical correlation analysis (CCA) was performed to separately explore the integrated effects between all the brain sources of gray matter variation and two sets of core autism symptoms."

<https://molecularautism.biomedcentral.com/articles/10.1186/s13229-020-00389-4>

"GLM analyses showed significant case–control differences for two independent components. The first component was primarily associated with decreased density of bilateral insula, inferior frontal gyrus, orbitofrontal cortex, and increased density of caudate nucleus in the autism group relative to typically developing individuals. The second component was related to decreased densities of the bilateral amygdala, hippocampus, and parahippocampal gyrus in the autism group relative to typically developing individuals. The CCA results showed significant correlations between components that involved variation of thalamus, putamen, precentral gyrus, frontal, parietal, and occipital lobes, and the cerebellum, and repetitive, rigid and stereotyped behaviors and abnormal sensory behaviors in autism individuals"

<https://www.spectrumnews.org/news/autism-brains-neurons-take-space-usual/>

"On average, the autism group has higher gray-matter volume in several brain regions, including the bilateral cerebellum, the insula and the anterior cingulate."

"The team did not find differences in gray-matter density at the whole-brain level or in individual regions. But the autistic participants had greater gray-matter volume overall. This is also the case in regions known to be different in people with autism, such as the superior temporal cortex, which is involved in language processing."

<https://www.google.com/amp/s/abcnews.go.com/amp/Health/Healthday/story%3fid=4509563&page=1>

"The excess gray matter in the parietal region may make it harder for autistic children to learn how to function socially by watching other people's behaviors, the researchers suggest."

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677578/>

"The savant syndrome is a rare condition in which persons with autistic disorder or other mental disabilities have extraordinary skills that stand in stark contrast to their overall handicap. Savant skills are typically confined to five areas: art, music, calendar calculating, mathematics and mechanical/spatial skills (Treffert 2005). These skills are accompanied by an exceptional ability to recall meaningless detail—memory without understanding (Sacks 2007) and a high incidence of absolute pitch (AP) and synaesthesia."

" Snyder & Mitchell (1999) argued that all savant skills, including AP and synaesthesia, reside within everyone, but that they are not normally accessible to conscious awareness. Owing to some atypical brain function, savants have privileged access to raw, less-processed information—information in some interim state before it is packaged into holistic labels. This privileged access facilitates a distinct literal cognitive style in which a person thinks in detail, working from the parts to the whole (De Clercq 2003). Savant skills are a form of reproduction. Savants access or read off something that exists in all of our brains, but is normally inaccessible through introspection (Snyder & Mitchell 1999). The precise neuroanatomical mechanism for gaining this privileged access is not yet resolved. It may be associated with an atypical hemispheric imbalance wherein concept networks are bypassed or inhibited."

" savant-like skills can sometimes be artificially induced in normal healthy individuals by inhibiting part of the brain—the left anterior temporal lobe (LATL). This is consistent with the notion that autistic savants have some atypical left brain dysfunction or inhibition together with right brain compensation"

" everyone has the raw information for savant skills, but it requires a form of cortical disinhibition or atypical hemispheric imbalance to be accessed."

" for savant skills residing equally within everyone is that they can emerge ‘suddenly and spontaneously’ (Miller et al. 2000, p. 86) in individuals who had no prior history for them, either in interest, ability or talent (Treffert 2006; Sacks 2007, pp. 157 and 313). Striking examples include skills in art, music (Sacks 2007), mathematics (Treffert 2006, p. 85), calendar calculating (LaFay 1987; Osborne 2003) and possibly AP (Zatorre 1989, see p. 573). The same appears to hold for synaesthesia (Sacks 2007, p. 180), as theory suggested (Snyder & Mitchell 1999), which is reported frequently by autistic savants "

" For instance, Sacks (1986) observed autistic twins who instantly guessed the exact number of match sticks that had just fallen on the floor, saying in unison ‘111’. "

" The savant syndrome is often associated with some form of left brain dysfunction together with right brain compensation, leading to a predilection for literal, non-symbolic skills"

" most savants are autistic and autism has sometimes been associated with a right-hemispheric bias (Herbert et al. 2005; Koshino et al. 2005) and a left hemisphere dysfunction"

" **while retaining the ability to recall object details (Mummery et al. 2000; Gainotti 2007). Oliveri et al. (2004) found that participants were less accurate in interpreting the meaning of opaque idioms (they became more literal) after rTMS to the left temporal lobe. "**

" My hypothesis is that savant skills are facilitated by privileged access to raw, less-processed sensory information, information that exists in all brains but is inaccessible owing to top-down inhibition. Thus, autistic savants tend to see a more literal, less filtered view of the world. Their ‘skill’ or performance does not depend on active learning, but simply on an effortless ‘reading off’ of this less-processed information."

" A fundamental bottleneck to creativity is our inability to join the dots up in novel ways. We have a predisposition to impose prior connections (§3c above). But, creativity would seem to require that we, at least momentarily, free ourselves of previous interpretations. Such literalness is a consequence of privileged access and thus gives insights into the so-called autistic genius (Snyder 2004) as well as hints to artificially enhance creativity"

<https://molecularautism.biomedcentral.com/articles/10.1186/s13229-018-0237-1>

"Heightened sensory sensitivity, obsessional behaviours, technical/spatial abilities, and systemising were all key aspects in defining the savant profile distinct from autism alone, along with a different approach to task learning."

" One final sensory link between autism and savant syndrome is the presence of synaesthesia, where stimuli such as letters, numbers, and sounds invoke automatic and additional sensory experiences such as colours [37, 38]. Hughes et al. [39] found that synaesthesia occurs at higher levels among autistic individuals with savant skills (but not those without savant skills)"

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677591/>

" proposed that eidetic memory may be important in savant syndrome, but this view is contradicted by the transformations that savants consistently perform on their material of expertise"

<https://www.researchgate.net/publication/348248663_The_savant_syndrome_and_its_connection_to_talent_development>

" The acquired form of the syndrome most often develops

following a fronto-temporal lesion on the left side of the

brain. Individuals suffering from the syndrome are typically

characterised by an outstanding memory ability

(photographic memory), which is not necessarily

accompanied by an ability to apply it in practice. "

" Synaesthesia, a type of hyper-connectivity, is a frequent

characteristic of the savant cognition"

<https://reader.elsevier.com/reader/sd/pii/S0160289696900203?token=E90D95B7AC58C499C11F81F8A46C4CD3A66EB05F8BBF4F17190FBCCFB87D2460AA0AA1455291C402F2CE8A9916037AB0&originRegion=us-east-1&originCreation=20220914200242>

"Savant and splinter skills are limited to music, arithmetic, and more complex mathematics, calendrical calculations, verbal representations, fine sensory discriminations, artistic ability, mechanical dexterity, and

memory for facts "

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3834557/>

" The hyper-connectivity hypothesis proposes that people with synaesthesia have excessive neural connections between different regions, connections that are diminished or absent from unaffected individuals [5,19-21]. Evidence for this hypothesis comes from a diffusion tensor imaging study [18] showing that people with grapheme-colour synaesthesia have increased white matter connectivity compared to unaffected controls."

" Daniel Tammet, who has both Asperger syndrome and synaesthesia, and who is a memory savant (he memorized Pi to 22,514 decimal places) inspired the hypothesis that savantism arises in individuals who have both autism and synaesthesia. This combination of conditions has been speculated to give rise to strong ‘systemizing’ and excellent attention to detail, both products of neural hyper-connectivity"