https://jme.bioscientifica.com/view/journals/jme/63/4/JME-19-0138.xml
Research on this protein is gaining momentum due to its potential as a target to combat neuropathic pain (Mei & Pasternak 2002, Corbera *et al.* 2006, Sun *et al.* 2016). Agonistic activity in the case of σ_1R may be indirectly measured by subcellular translocation, establishment of protein-protein interactions or regulation of ion channel activity (Wu & Bowen 2008, Kim *et al.* 2010, Navarro *et al.* 2010, Su *et al.* 2010). Indirect evidence also shows the involvement of σ_1R in neurological disorders such as depression (Su *et al.* 2010). Also interesting is the correlation between a mutation in the receptor and debut and progression of juvenile lateral amyotrophic sclerosis

https://rarediseases.info.nih.gov/diseases/11901/juvenile-amyotrophic-lateral-sclerosis
- possibly what toto has that no doc can figure out (1000 cases in us so lack of diagnosis so far makes sense bc rare)
- facial spasticity more frequently affects women

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4415495/
“ a growing body of work indicates that several factors (e.g., low self-esteem, sense of internal control, self-enhancement, emotion intolerance, self-centeredness) may cooccur and affect the narcissistic individual’s empathic capability and functional pattern”

“further qualified this narcissism–empathy relationship, suggesting that there could be separable aspects of ability and willingness that affect narcissistic individuals’ empathic functioning. That is, some narcissistic individuals may have intact empathic ability, but choose to disengage from others’ pain or distress, while others may have a deficient ability in the recognition of others’ feelings”

“For NPD, the following conceptualization of empathic functioning was suggested: “Impaired ability to recognize or identify with the feelings and needs of others; excessively attuned to reactions of others, but only if perceived as relevant to self; over- or underestimate of own effects on others.””

https://pubmed.ncbi.nlm.nih.gov/23586919/
“ALS patients showed defective emotional empathy attribution, related with reduced grey-matter density in the anterior cingulate cortex and right inferior frontal gyrus”

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243720
“Later WE wake up time and WE delay in wake up time correlated with measures of externalising problems ($p<0.001$), whilst a larger WE delay in wake up time was correlated with lower internalising problems ($p<0.001$” WE: mean wake up times”

“The present findings confirm and extend our previous findings that sleep patterns in adolescents from the general population correlate with regional brain grey matter volumes and psychological functioning. In particular, later WE wake up times were associated with lower GMV in the mPFC and the amygdalae as well as with externalising symptoms. Smaller grey

matter volumes in the mPFC region were associated with increased cognitive impulsivity as well as internalising and externalising problems”

“Overall, the present findings are consistent with and extend our previous report in 14 year-old adolescents, suggesting that the negative impact of a later weekend wake up time on the adolescent brain can result in reduced ability to regulate emotions”

https://pubmed.ncbi.nlm.nih.gov/15617536/
“melatonin improved sensory and motor neurobehavioral outcomes by 47 and 30%, respectively ($P<0.01$). Thus, delayed (1 hr) treatment with melatonin reduced both gray and white matter damage and improved neurobehavioral outcomes following transient focal cerebral ischemia in mice. The finding of reduced oxidative damage observed with melatonin suggests that its major mechanisms of action are mediated through its antioxidant and radical scavenging activity.”

- AUTHOR SIDE NOTE: A malignant narc i lived with tried a melatonin and they said it made her feel funny and off for a day and got mad i offered her it (once it wore off)

https://pubmed.ncbi.nlm.nih.gov/15673559/
“when given at the time of ischemia or reperfusion onset, melatonin reduces neurophysiological deficits, infarct volume, the degree of neural edema, lipid peroxidation, protein carbonyls, DNA damage, **neuron and glial loss**, and death of the animals. Melatonin's protective actions against these adverse changes are believed to stem from its direct free radical scavenging and indirect antioxidant activities, possibly from its ability to limit free radical generation at the mitochondrial level and because of yet-undefined functions. Considering its high efficacy in overcoming much of the damage associated with ischemia/reperfusion injury, not only in the brain but in other organs as well, its use in clinical trials for the purpose of improving stroke outcome should be seriously considered. “

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4241182/
GLIAL ETC. SHIT; POSSIBLE CONNECTION TO THE EXCESS GLUTAMATE PROBLEM
“Astrocytes are ectodermal cells involved in ion homeostasis, neurotransmitter recycling and metabolic support to surrounding neurons. One of the most important and extensively studied supportive functions of astrocytes is their involvement in the glutamate-glutamine cycle”

“Uptake of glutamate from the synaptic cleft between presynaptic and postsynaptic neuron through glutamate transporters EAAT2 (GLT-1 in rodents) and EAAT1 (GLAST in rodents) expressed by astrocytes will prevent excessive postsynaptic stimulation of glutamate receptors and motor neuron cell death, a process which is called glutamate mediated excitotoxicity.”

- Note: memantine is the most effective thing to combat glutamate excitoxicity and [redacted] likes 300 mg a day

“When astrocytes encounter any biological hazard in their immediate surroundings, astrocytes become reactive and increase the expression of some astrocyte markers (e.g. GFAP and ALDH1L1) in a process called astrogliosis.”

“In the brain of ALS patients, astrogliosis is seen in both the grey as well as white matter and not limited to the motor cortex (Kushner et al., 1991; Nagy et al., 1994). In the spinal cord of ALS patients, there is an enhanced astrocytic reactivity in the ventral horn, dorsal horn and the regions where the corticospinal tract fibers enter the grey matter “

“In ALS rodent models and to a lessor extend in ALS patients, the BBB is disrupted, characterized by upregulation of adhesion molecules and downregulation of tight junction proteins”

https://www.imedpub.com/articles/the-cognitive-neuroscience-of-narcissism.php?aid=22149
“It was Kohut [6] who first introduced the term narcissistic personality disorder (NPD) and went on to take some of Freud's earlier ideas about narcissism and expand upon them. Narcissism played an important role in Kohut's theory of self-psychology, which suggested that narcissism allows people to suppress feelings of low self-esteem and develop a positive sense of self. Essentially, Kohut’s theory centers on the development of two archaic narcissistic configurations: 1) the “grandiose self”, an exhibitionistic “I am perfect” image of the self, which represents an archaic “normal” primitive self (not a pathological structure as for Kernberg); and **2) the idealized parent image or omnipotent object, whereby perfection is ascribed to an admired self-object, the “you are perfect but I am part of you” view of the parent** [7].”
- Author note: Type 2 is more advanced and probably indicates higher IQ and EQ

““social psychologist Erich Fromm first coined the term **"malignant narcissism" describing it as a "severe mental sickness" representing "the quintessence of evil"**. He characterized the condition as "…t**he most severe pathology and the root of the most vicious destructiveness and inhumanity.”** Fromm's personality theory rests on data he gathered from a variety of sources, including psychotherapy, cultural anthropology, and psychohistory. Fromm applied the techniques of psychohistory to the study of several historical people, including **Adolf Hitler--the person Fromm regarded as the world's most conspicuous example of someone with the syndrome of decay, which includes necrophilia, malignant narcissism**, and incestuous symbiosis.”
- Malignant narcissism and psychopathy were used interchangeably in the 70’s

“While **narcissists are common, malignant narcissists are less common. A notable difference between the two is the feature of sadism**, or the gratuitous enjoyment of the pain of others. A narcissist will deliberately damage other people in pursuit of their own selfish desires, but may regret and will in some circumstances show remorse for doing so, while **a malignant narcissist will harm others and enjoy doing so, showing little empathy or regret for the damage they have caused. People who are high in this trait fail to help others unless there is immediate gain or recognition to themselves for doing so; often think they are above the law and therefore violate it;** and readily trample over others in their efforts to rise to the “top,” which are where they think they belong. They are generally incapable of forming the kinds of deep, meaningful, lasting relationships with others that we all need in order to live happy, emotionally secure lives.”

“Within the dimension of interpersonal functioning, we find most of the descriptors originally included in DSM-III-R, though with slightly different wording. Descriptors such as “little genuine interest in others” (i.e., exploitive) and “relationships largely superficial and exist to serve self-esteem regulation” (i.e., believes he/she is “special”) are used to the depict problems with intimacy. Descriptors such as “excessively attuned to reactions of others” (i.e., overreacts to criticism) and “impaired ability to recognize or identify with the feelings and needs of others” (i.e., lacks empathy) are used to depict problems with *empathy*. The older criteria of grandiose self-importance, sense of entitlement, and arrogant/haughty attitudes are now grouped together under *grandiosity*. The older criterion of “requires excessive admiration” is listed under *attention seeking*. The only item to be omitted from the new nosology is “often envious of others”. In addition to a more highly organized format, a dimensional set of criteria with diagnostic thresholds based on empirical data [25,26] can be found in DSM-5 Section III: Emerging Measures and Models. Given the flexibility and comprehensiveness of this new diagnostic system, the DSM-5 functions as an important resource for identifying pathological narcissism.”

- INFO FOR ME (NOT ON TOPIC) “Most estimates are that there may be over one hundred billion individual nerve cells, or neurons, in the human brain. Each of them can make up to several thousand connections with other neurons to form what can practically be considered an nearly infinite network of nerve cell activity. These neurons are organized into very specific regions with very specific functions and these regions are also highly interconnected to form an extraordinarily complex series of integrated functional groups.”

“We know that the front part of the brain, the frontal cortex, regulates much of our thinking and reasoning abilities. Similarly, around the lower sides of the brain are areas called the temporal lobes, where we find the keys to controlling many emotional states including fear and anger.”

INFO FOR ME “It is intriguing to note that consistent evidence shows that sharing the emotions of others is associated with activation of neural areas that are also active during the first-hand experience of that emotion. For example, one recent study showed that patients with lesions caused by removing brain tumors in the anterior insular cortex (AIC) had deficits in explicit and implicit empathetic pain processing [39]. This study provides evidence suggesting that the empathy deficits in patients with brain damage to the AIC are surprisingly similar to the empathy deficits found in several psychiatric diseases, including autism spectrum disorders, borderline personality disorder, NPD and others, suggesting potentially common neural deficits in those psychiatric populations.”
- Insular cortex is associated with multiple sensory systems and “Insular neurons also respond to stimulation of the vagus nerve”

“For the **NPD group, this region of the cerebral cortex was markedly reduced in thickness** compared to the control group. **The amount of empathy was directly correlated to the volume of gray matter in the insular region.** Overall, **patients with narcissism exhibited a significant reduction of gray matter in the insular cortex** “

- Author side note: performing mathematics increases grey volume (have to double check what brain region it does this but i think everywhere)

“neuroimaging data indicates lower activity in the insula in high narcissistic subjects”

****”**Higher narcissism scores were associated with lower connectivity between certain brain areas, including the prefrontal cortex and ventral striatum.”**
- Author comment: NSI-189 to increase connectivity between different brain areas? Seems like it would help. Research on alternative approaches to increase brain region connectivity required

“the insula has been singled out as the critical neural substrate for interoceptive and emotional awareness”

“It is associated, at least in part, with brain irregularities primarily within the insular cortex and also in the frontal lobes of the brain. These are critical areas associated with the ability for empathy and higher level processing, judgment and decision making.”

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7965387/
“Prefrontal lobe degeneration exists in patients with ALS as indicated by an abnormal mesial prefrontal cortex neurochemical profile”

“cerebral degeneration beyond the motor cortex involving frontal and temporal lobes gives rise to mild cognitive and behavioral impairment in upward of 50% of patients”

“ALS patients with impaired verbal fluency have functional and structural imaging abnormalities in the frontotemporal region, including the anterior cingulate”

“ALS patients with impaired verbal fluency have functional and structural imaging abnormalities in the frontotemporal region, including the anterior cingulate where our voxel was placed: functional MR imaging has demonstrated impaired activation in the dorsolateral PFC and anterior cingulate gyrus during a letter fluency task,[33] and white matter volume is reduced in motor and nonmotor associative tracts in frontotemporal regions and the cingulum”

“Mesial PFC dysfunction is associated with behavioral changes in addition to cognitive impairments, including apathy and disinhibition”