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Is There a Relationship of Mirror Neurons with Creudzfelt-Jakob Disease?

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ABSTRACT

Objective: To study the association between the mirror neuron system and Creutzfeldt-Jakob Disease.

Materials and Methods: A comprehensive search was performed in various databases including popular neurology and neuropsychiatry journals. In total 800 articles were reviewed with 682 excluded due to the inclusion-exclusion criteria.

Results: Creutzfeldt-Jakob can lead to a number of different pathology including dementia, depression, personality changes, cognitive inadequacy, incoherent speech, sleep issues, motor deficit and other movement disorders. When studied independently each of these symptoms characteristically activated certain parts of the brain, visualized in neuroimaging. Coincidentally, the same brain areas were found to be independently affected by the mirror neuron system, indicating that these symptoms could be associated with mirror neuron dysfunction. It can, therefore, be hypothesized that a connection between mirror neurons and Creutzfeldt-Jakob disease exists.

Conclusions: Many of the symptoms and complications involved in Creutzfeldt-Jakob disease are found to be associated with the mirror neuron system.

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Keywords: Mirror Neurons, Creudzfelt Jakob and mirror neurons, Creutzfeldt-Jakob Disease (CJD) and Mirror Neuron System (MNS), legs and mirror neurons, limbs MNS, movement MNS.

1. Introduction:

Creutzfeldt - Jakob disease, abbreviated CJD, is an infrequent, slow acting, degenerative neurological disease that currently has no cure and is always fatal (Fernández-Borges et al., 2015). CJD is thought to be caused by an infection of Prions, or protein containing particles which lack measurable amounts of nucleic acid. The Prions thought to be involved in CJD fall under the category of "Slow" Infectious diseases due to their effect time, a category which includes conventional viruses and bacteria along with unconventional particles. A unique aspect of prions is that they are cooking temperature resistant, providing a reason as to why they are suspected to be transmitted through food. The proteins that Prions consist of are naturally present in cells, encoded by the normal cellular PRNP (Prion Protein) Gene, and are assumed to be involved in signal transduction in neuronal cells. Prion Proteins in healthy cells, or PrPC (Prion Protein cellular), are known to have an alpha-helical conformation. Infectious Prion Proteins, or PrPSC (Prion Protein Scrapie), however, have a beta-pleated sheet conformation which has been observed to cause abnormal aggregation into filaments which disrupt nearby neuron function and eventually leads to cell death. PrPSC Prions also have the capability to change the conformation of normal alpha-helical Prion protein (PrPC) and thus "reproduce" in this manner. Both forms have been found to contain the

same amino acid sequence differing only in their respective conformations.

CJD, along with other human prion-mediated diseases such as Kuru or Gerstmann-Sträussler-Scheinker syndrome, additionally falls within the category of Transmissible Spongiform Encephalopathies or TSEs. This categorization is due to the appearance of "spongy", cheese-like holes within brain parenchyma caused by neuronal cell death. In fact, the transmissibility of Prions was first discovered when infected brain parenchyma from humans was transferred to the brains of primates and then serially transferred to other primates. It was at this time where it was seen that Prion diseases could also be obtained through ingestion of infected tissue, however the Prion protein had to survive intestinal digestion and have the ability to penetrate gut mucosa before amplifying itself within follicular dendritic cells in lymphatic tissue, such as Peyer's patches, and eventually spreading to the brain.

There are three main types of Creutzfeldt – Jakob disease, Variant CJD, Familial CJD, and Sporadic CJD, each categorized by the process in which they develop. Variant or Infectious CJD is a transmissible form of CJD, thought to be due to ingestion of contaminated food, whereas familial CJD is an inherited, or genetic, form of CJD, with Sporadic CJD being neither infectious nor hereditary and accounting for a majority of CJD cases. Familial CJD is thought to be due to a mutation in parents' germ cells while Sporadic CJD is hypothesized to be a result of somatic mutations within a diseased individual. CJD may also arise iatrogenically as a result of contamination with infected tissue in procedures including blood transfusion, use of human-derived pituitary growth hormones, gonadotropin hormone therapy, and corneal and meningeal transplants (Johnson, 2005; Comoy et al., 2015).

Aside from the three main types of CJD, alternative forms have been found to exist although they are extremely rare and tend to arise within a certain locality. Detailed within Great Britain and France, a form named New Variant Creutzfeldt - Jakob disease (nv-CJD) is known to arise within younger individuals, as compared to standard CJD, and is characterized by Psychiatric illness and the slightly longer onset of death (Kobayashi et al., 2015). This form is similar to that found in Japan called the Panencephalopathic form where symptoms appear to slowly advance for several years, before a relatively long onset death. Scientists are currently unable to determine what factors lead to the observed variations in the course and symptoms of the disease.

One of the most apparent symptoms and the mark of CJD is that of rapidly progressive and sudden dementia. At first, patients may begin to encounter weakening of motor skills and difficulty in performing standard movements, along with impaired vision. Eventually, family members and close relatives will notice personality changes, followed by depression, impaired judgment, memory, and formulation of thought. In the latter stages of CJD, mental deterioration becomes critical, leading to myoclonus, blindness, and the inability to communicate or move, coupled with a weakening immune system, allowing for infections such as Pneumonia to cause a fatality (Zivkovic, et al., 1999).

About one in every million individuals are affected by CJD across the globe annually (Ohashi et al., 2014), and no correlation has been found between dietary habits, animal exposure, or occupation and increased susceptibility to the disease. Both meat eaters, who may come in contact with animals affected by prion disease, and vegetarians have the same risk associated with CJD. In countries where animals show obvious signs of infection, such as scarring due to Scrapie, the age of onset of CJD, about sixty years of age on average, remains the same with ninety percent of individuals passing within a year.

Although symptoms of CJD are often clinically homologous with many progressive neurological disorders such as Alzheimer's or Huntington's disease, CJD can be clearly distinguished during an autopsy due to the unique brain tissue changes that occur. Additionally, the almost immediate loss of a patient's motor and judgment skills following prion infection signals that CJD is occurring. CJD, aside from causing the conversion of normal alpha helix Prion protein to beta pleated sheets, may also have some association with mirror neurons (Zhang et al., 2016).

Mirror Neurons are a type of neuron that was first identified in the inferior parietal lobule and the ventral premotor cortex in a macaque monkey utilizing single cell recording (Rizzolatti et al., 1996). These neurons were found to undergo stimulation both when the monkey performed a specific action, such as reaching for an object, and whilst noticing the execution of said action by another. Mirror Neurons were later identified in humans and assumed to be involved in social cognition, although their specific role is unclear (Cattaneo & Rizzolatti, 2009; Keysers & Gazzola, 2010; Wudneh et al., 2016; Saffin & Tohid, 2016). The development of ALS has also been found to relate to mirror neurons (Eisen et al., 2014).

Although little research has been done on the relationship between Creutzfeldt – Jakob disease and Mirror neurons, certain studies have shown that there may be an association between the two. This paper aims to review and summarize that research and

determine if a plausible relationship between Mirror Neurons and Creutzfeldt – Jakob disease may exist.

2. Materials and Methods:

A comprehensive review of published literature was conducted using PubMed, Wiley Online Library, and Science Direct. No data restrictions were implemented. In total 800 articles were reviewed, and 682 were excluded due to the inclusion-exclusion criteria. The criteria included articles from high impact factor journals indexed in Medline. Also, studies after the year 1950 with human subjects or systematic reviews emphasizing prion proteins, Creutzfeldt-Jakob Disease and Neurodegeneration were included. Mirror neuron articles after the year 1990 were also included and most studies were human or animal studies with neuroimaging results.

Reference sections were reviewed for additional articles. Titles and abstracts were assessed to determine if articles were relevant. In total, over eight hundred article titles and abstracts were reviewed; one-hundred articles were chosen for inclusion in the final paper. Data was obtained from descriptions of research projects, experiments, program evaluations, systematic reviews, and case series.

4. Results and Findings:

The results show that the Mirror Neuron System may, in fact, have an association with Creutzfeldt-Jakob Disease and potentially a number of additional neurodegenerative diseases. Patients with CJD are known to exhibit Issues with Muscular coordination, Dementia characterized by Impaired Cognitive Ability related to Memory or Acquiring knowledge/Understanding through thought, experience, or senses, Personality changes, including impaired memory, judgment, and thinking, Depression, and Movement Disorders including jerky limb movements, random muscle twitching, stiffness, inability to perform controlled movements, and dysarthria. Although previously the association of mirror neurons with CJD was not comprehensively studied certain evidence points towards a connection between CJD and Mirror Neurons.

According to some studies when people perform an action, imagine, or observe movements, mirror neurons fire asynchronously reducing the power of the mu band. The main areas of the brain where mirror neurons have been found are the premotor cortex, inferior parietal cortex, and the superior temporal sulcus STS. The parietal cortex is also considered to be important in representation and interpretation of the objectives of the observed action. There may also be a correlation between the development of visual perception and sensorimotor development. Interestingly all of the above areas are found to be affected in by CJD hinting at a possible link between CJD and mirror neuron system. Figure 1 and 2 show a simple representation of this.

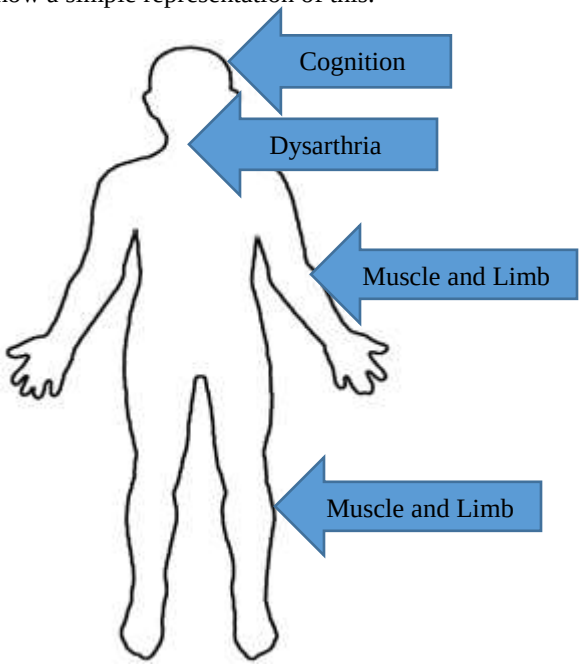

Figure 1. Functions known to be affected by Creutzfeldt-Jakob Disease.

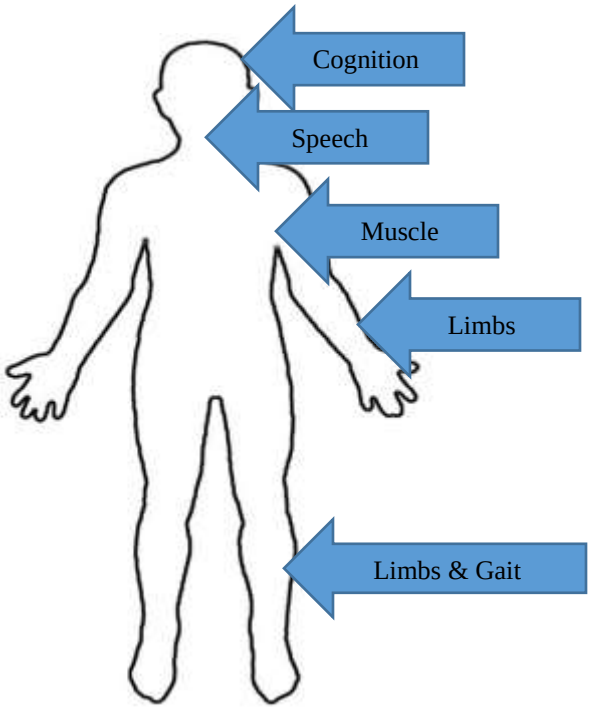

Figure 2. Functions thought to be associated with mirror neurons.

5. Discussion:

5.1. Muscular coordination and mirror neurons

Although it was initially assumed that the Mirror Neuron System was involved in merely the imitation of the observed actions of another, due to the fact that Mirror Neurons are known to be activated during the observation of an action and the execution of said action, current theories suggest that Mirror Neurons are actually involved in the understanding and learning of respective actions. In this theory, Mirror Neurons take part in the creation and maintenance of neuronal pathways related to observations and "teach" the brain how to act, and whether or not it should be leading to "choice" (de la Rosa et al., 2016). This may be why infants and young children seem fascinated by certain stimuli including the changing expressions on faces, the movement of others' hands, feet, bodies, their own hands or feet in motion, and the surrounding environment (Casile et al., 2011). EEG mu wave desynchronization that occurs whilst observing performance of motor actions and abstract motions has also been found in infants following action observation, in the same moments where it is assumed that learning/formation of motor skills is taking place (Virji‐Babul et al., 2012). This desynchronization has been used to separate populations of sensory and motor neurons and supports the existence of mirror neurons which are simultaneously activated during the action observation that causes EEG mu wave desynchronization (Braadbaart et al., 2013; Mukamel et al., 2010]. As such it can be assumed that mirror neurons are involved in activations of the motor cortex, or muscular coordination/motor skills.

In a study performed by the Chang Gung Memorial Hospital, subjects were shown footage of an actor initially standing completely still, followed by an egocentric style of walking. Using the help of functional Magnetic Resonance Imaging, activation of neurons in the motor cortex was observed, during the same time where Mirror Neuron activation was occurring, at the sessions where the actor was walking (Wang et al., 2008), indicating a relationship between the two. This relationship was further corroborated by a study where Lateralized Readiness Potential, or the electrophysiological correlate of premotor activation in the primary motor cortex, was used with evoked hand movements and additional potential was observed during the viewing of self-made movements through mirrors as compared to the movements themselves (Touzalin-Chretien & Dufour, 2008). Some scientists disagree with this relationship due to the order dependent lack of symmetry in the area based neuronal activation observed, however, this may be due to a number of different factors and does not necessarily indicate the lack of a relationship (Lingnau et al., 2009). Mirror Neurons may have a part in the buildup, maintenance, and "learned" aspect of muscular coordination and observed inactivation of mirror neurons in CJD may, in fact, have a role in patients' issues with muscular coordination.

Table 1: *Mirror Neuron System relationship to Muscular coordination.*

CREUTZFELDT-JAKOB DISEASE	MIRROR NEURONS
Issues with Muscular coordination	1) Mirror Neurons may take part in the creation and maintenance of "learned" neuronal pathways related to muscle movements, MNS inactivation leads to issues. 2) Infants at birth attracted to specific sets of stimuli, including faces, hands, and surroundings in motion which mirror neurons may be involved in and can explain CJD patients' difficulty in learning. 3) EEG-mu rhythm DE synchronization has been shown in infants during action observation in the process of learning, which does not take place in CJD patients. 4) Increased mirror neuronal activation when observation and execution taking place as compared to mere execution, implies potential treatment.

5.2. Dementia and mirror neurons

Based on recent research and the utilization of different neuroimaging techniques, it is now known that the activation of the Mirror Neuron System occurs both during the execution and observation of an action and that this system is involved in a number of different cognitive functions (Di Pellegrino et al., 1992). In fact, during a study conducted P. Rattanachayoto et al. where subjects were presented with a video of a piece of paper being torn and asked to watch the video and then stare at a fixed point, significant activation of the bilateral front lobe and inferior parietal lobe occurred during video watching (Rattanachayoto et al., 2012), similar to additional studies (Buccino et al., 2001; Decety et al., 2002). However, in individuals with impaired cognitive ability specifically related to the bilateral frontal lobe, such as Alzheimer's disease patients, significantly less mirror neuron activation occurred as the patients proceeded to forget the contents of the video,

implying a relationship between mirror neurons and memory formation/upkeep.

Additionally, according to V.S. Ramachandran, mirror neurons are involved in aiding an individual's anticipation of the actions of another, activating neuronal pathways related to said actions and associated emotions (Ramachandran, 2012). Ramachandran believes that the activation of mirror neurons allows for the consideration of others' point of view and construction of "a mental model of another person's complex thoughts and intentions", leading to the ability to feel empathy with them (Hannon, 2013). This also may allow for the sensation of self-consciousness, as when an individual is able to note that another is conscious of a certain facet of them, mirror neurons activate the same pathways within the individual that are assumed to be activated in the other.

Dementia is generally characterized by progressive memory impairment attributable to cognitive decline (Kester & Scheltens, 2009). Dementia patients often struggle with everyday activities due to this fact and in later stages may have difficulty performing certain motor actions. In was noted though in a study by Joanna G Douma et al. that when elderly patients with dementia residing in care facilities were shown footage of individuals walking, observation of the action had facilitative effect on the execution of the action, in this case walking (Brass et al., 2000; Douma et al., 2015). Moreover, activation of mirror neurons during observation has also been found beneficial in reestablishing motor functions in phenomena such as stroke (Small et al., 2012). Mirror Neurons may also play a role in emotional stability aside from empathy, as dementia patients often have difficulty understanding their surroundings and the feelings of those around them, physically manifested in fewer mirror neuron activations (Rattanachayoto et al., 2012).

Table 2: *Mirror Neuron System Relationship to Dementia.*

CREUTZFELDT-JAKOB DISEASE	MIRROR NEURONS
Dementia – Impaired Cognitive, Ability related to Memory or Acquiring knowledge / Understanding through thought, experience, or senses.	1) Fewer Mirror Neuron System activations in patients with cognitive impairments compared to controls. 2) Dysfunction of normal feelings of Self-Consciousness thought to be attributed to Mirror Neurons. 3) Observation of actions and respective Mirror Neuron activation was seen to have a facilitative effect on the execution of the observed action as has been found for movement onset. 4) Activation of the MNS shown beneficial for rehabilitation of functionality in areas presumed dead, such as a motor function in areas affected by stroke.

5.3. Personality Changes

Currently it has been established that Mirror Neurons may be involved in the "learning" of motor activities and the associated "choice" related to them (Bonini & Ferrari, 2011; Caggiano et al., 2012), and the observation of an action followed by the understanding/prediction of the course of said action and corresponding phenomena (Kilner et al., 2007). However, the discovery of mirror neurons in regions of the brain that are known to be involved in Perception, or the unconscious psyche/personality based interpretation of sensory information, rather than the mere acquisition of sensory information, hints that mirror neurons may also be involved in social cognition (Rizzolatti & Sinigaglia, 2008).

In fact, in a study by Wicker et al. activity in the same brain regions was found both when individuals smelled something they thought was disgusting and observed others making disgusted faces (Wicker et al., 2003). Additionally in a study by Rizzolatti et al. where individuals' brain activity was recorded in three instances - when observing hand grasping without context, when observing hand grasping for the purpose to picking up a mug to drink, and when observing hand grasping for the purpose of cleaning a mug – increased mirror neuron regional activity was present in the two context filled instances suggesting the role of mirror neurons in more than just action observation but awareness of purpose/intention as well (Iacoboni et al., 2005). Interestingly enough it has also been noted that greater mirror neuron activation occurs when observing another individual executing an action as compared to a robotic or computerized model hinting that mirror neurons may be involved in a sort of intraspecies communication (Fu & Franz, 2014).

Similarly, in a series of experiments that aimed to explore the neurological components related to marketing, consumer understanding, customer orientation, and product recall, a relationship with mirror neurons was found. Weber et al. noted that mirror neurons were essential for consumer learning in a marketing environment as mirror neurons allowed for a vicarious learning experience and greater product desirability (Weber, 2007). On the flipside Bagozzia et al. found a positive correlation between mirror neuron activation and individual salespersons'

customer orientation, or understanding of customers' needs/wants/desires (Bagozzi et al., 2012). It was also found that mirror neuron activation differed amongst individuals for the same activities and that the strength of customer orientated salespersons could be based on increased mirror neuron efficiency (Lacoste-Badie & Droulers, 2014). Iacoboni et al. additionally found that actions with perceivable intentions related to advertised products cause greater mirror neuron activation and stronger product recall as compared to merely observing the advertised product and even seemingly small differences could be registered by the brain (Iacoboni et al., 2005; Ohme et al., 2009) forming a conceivable relationship between mirror neurons and understanding others. Mirror Neurons may be involved in Perception, Social Cognition, Intent Based Understanding, and the formation of memory - all factors which shape an individuals' personality – and the impairment of such a system might provide insight as to the personality changes and impaired judgment/thinking present in CJD.

Table 3: *Mirror Neuron System Relationship to Personality Changes.*

CREUTZFELDT-JAKOB DISEASE	MIRROR NEURON CHANGES
Personality changes, including impaired memory, judgment, and thinking	1) Mirror neurons present in regions of the brain involved in Perception and may be involved in social cognition. Fewer activations may cause difficulty in interpersonal understanding and respective responses. 2) Mirror Neurons may be involved in understanding the intention of others which lead to personality based responses that are lacking in CJD. 3) Communication has also been found to have a relationship with mirror neurons and impairment of the Mirror Neuron System may underlie difficulty in early stage CJD patients' performance of this task. 4) Functioning of MNS differs across people related to customer orientation (understanding wants of the customer) which could reflect one's personality towards another.

5.4. Depression and mirror neurons

Although Depression can generally be characterized by sleep changes, lack of interest, feelings of guilt, lack of energy, decreased cognitive ability, changes in appetite, psychomotor retardation, and suicidal thoughts or intentions, one of the prime factors in the onset of depression is emotional instability. Many Depression patients are known to experience decreased neurological responses to pleasure and pain along with an inability to possess empathy, both in regards to the feelings of others and their own, potentially explained by the fact that the Anterior cingulate cortex and anterior insular cortex, which are known to be negatively affected by depression, are believed to formulate empathy (Singer, 2006).

Additionally, studies have shown positive correlations between individuals capable of stronger expressions of empathy and greater mirror neuron activation, along with fewer mirror neuron activations in patients who had the inability to empathize with others (Acharya & Shukla, 2012; Zaki & Ochsner, 2012).

In fact, in a study by Mehta et al. aberrant brain activity, dysfunction in the mirror neuron system in the right inferior parietal cortex, and decreased mirror neuron activation was present in patients with psychological disorders, namely schizophrenia, and this was implicated in depression as well (Mehta et al., 2014).

Therapy revolving around the Mirror Neuron System has also been shown to be beneficial for individuals with emotional disorders and is thought to be related to fixing issues related to the social aspect of emotion that is lacking including understanding others and empathy (Ferrari & Rizzolatti, 2014). Persistent anxiety due to this phenomenon may also lead to insomnia or sleeplessness observed, which the MNS may relate to (Haker et al., 2013). Mirror Neurons are said to have an effect on depression independently, and this is likely true as well for CJD patients suffering from depressive tendencies/depression.

Table 4: *Mirror Neuron System Relationship to Depression.*

CREUTZFELDT-JAKOB DISEASE	MIRROR NEURON CHANGES
Depression	1) People who are more empathic have stronger activations of the mirror system and similarly, individuals' incapable of expressing empathy has decreased mirror neuron activation. 2) Uncoupling of mirror neuron circuits in depressed people may make them feel more isolated and unable to relate to friends and loved ones. 3) Decreased/impaired mirror neuron function was observed in schizophrenia patients and implicated in patients with other psychological disorders, may also be present in CJD.

5.5. Movement disorders

Although scientists have identified the relationship of mirror neurons to the primary motor cortex and the development/learning" of motor skills, the specific role of the mirror neuron system in the maintenance, stabilization, or prevention of unwanted motor activation has not been fully explored. In the later stages of CJD, patients are known to experience dysarthria, jerky limb movements, random muscle twitching, stiffness, and inability to perform controlled movements, along with a number of activation/inactivation related movement disorders, and this is thought to be attributed to motor neuron dysfunction (Zivkovic, et al., 1999). Interestingly, however, in an experiment done on the macaque monkey that visualized mirror neuron and mirror-like activity of the pyramidal tract neurons in the primary motor cortex it was additionally observed that a certain portion of the cortico-motoneuronal pyramidal tract mirror neurons was suppressed during action observation (Kraskov et al., 2014).

Cortico-motoneuronal pyramidal tract suppression is thought to be involved in withholding unwanted movement and preventing unintentional overflow of neuronal activity (Schieber, 2011). In fact, it was reported that specific groups of pyramidal tract mirror neurons had a facilitative effect on muscle activity during action observation while others may have had a suppressive effect, and during activation of these "suppressive" mirror neurons a complete absence of related muscle activity was observed (Vigneswaran et al., 2013). These "suppressive" mirror neurons may be involved in ensuring conflicting signals or muscle activation does not take place during activation of "facilitative" mirror neurons or ensuring that "facilitative" mirror neurons are not active during unintentional movement, and in groups of dancers greater "facilitative" mirror neuron activation has been shown during action observation of highly trained specific intentional movements (Calvo-Merino et al., 2005).

Through fMRI Mirror Neuronal activity can be visualized in the left dorsal premotor cortex, bilateral precentral gyrus, the supplementary motor area, the ventral premotor cortex or "visuomotor grasping circuit", and other cortical and subcortical areas aside from the primary motor cortex and this may provide clues as to where "suppressive" mirror neurons are present (Wang et al., 2008; Alegre et al., 2010). It is important to note that these mirror neurons require full view action observation and goal-directed behavior and can utilize smell and hear aside from mere observation similar to previously established mirror neurons (Nelissen et al., 2011; Enticott et al., 2010). Neuronal responses may also take place in response to robotic actions, although limited in comparison to that of a human's actions (Gazzola et al., 2007; Peeters et al., 2009). As such malfunction of the mirror neuron system as a whole may delineate the jerky, unstable movement disorders present in later stage CJD patients, and provide cause to the dysarthria and respective slurred speech observed.

Table 5: *Mirror Neuron System relationship to Movement Disorders.*

CREUTZFELDT-JAKOB DISEASE	MIRROR NEURON CHANGES
Movement Disorders including jerky limb movements, random muscle twitching, stiffness, inability to perform controlled movements, and dysarthria.	1) Mirror-like activity seen in Pyramidal Tract Neurons (PTNs) and certain portions of the cortico-motoneuronal pyramidal tract mirror neurons were suppressed during action observation, may be involved in suppression of unwanted activity. 2) Activation of Suppressive Pyramidal Tract Mirror Neurons linked to the absence of related muscle activity, a malfunction in CJD may relate to unwanted motor activation during previously learned movement. 3) Mirror neurons highly active during action observation of highly trained intentional movements, deactivation may cause issues with the execution of movement.

5.6. Parts of the Brain commonly involved in CJD and the mirror neuron system

Aside from symptomatic evidence, the location may also provide affirmation of a potential relationship between CJD and the mirror neuron system. Neuroimaging studies involving patients afflicted with CJD have shown damage in regions of the brain including the Basal ganglia, thalamus, hippocampus, frontal and paracentral motor cortex, cerebellar vermis, and major portions of the premotor and primary motor cortex along with observable reductions in the volume of frontal and parietal gray matter (Caine et al., 2015). These areas and especially the premotor cortex, primary somatosensory cortex, supplementary motor area, and inferior parietal cortex have indicated the presence of mirror neuronal activity and may provide an explanation for the symptoms observed in CJD (Molenberghs et al., 2009).

Table 6: *Articles showing the presence of mirror neurons and relationship to activities/locations affected by CJD.*

Author/ Publication year	Population	Sample size	Main findings
Rattanachayoto P. et al, 2012	Eighty cognitively normal subjects, 5 patients with MCI, and 7 patients with mild AD	92	While being scanned with fMRI, subjects were asked to view a video of a piece of paper tearing. In the normal group, MCI group and mild AD group activations were observed. Those observing hand movement had significant activations of bilateral inferior frontal lobule and inferior parietal lobule.
Mukamel R. et al, 2010	Twenty-one patients	21	Discharge observed during both the observation and execution of one type of action.
Wang et al, 2008	Twelve right-handed gender-balanced subjects aged between 18 and 25 years were investigated.	12	Using fMRI activation detected in many motor-related areas including supplementary motor area, bilateral precentral gyrus, left dorsal premotor cortex, and cingulate motor area. Smaller additional activations were observed in the bilateral precuneus, left thalamus, and part of the right putamen.
Touzalin-Chretien & Dufour, 2008	Eleven healthy paid volunteers (five males, six females; mean age 27.7 yr.) were enrolled in the experiment	11	Most evoked potentials were noted when mirror placed in the inactive hand while the opposite hand performed the task.
Fu & Franz, 2014	Eighty-four right-handed healthy adults (40 males and 44 females; mean age = 20.9 years	84	Significant frontal cortex activity found during action observation, while these effects at frontal MNS sites completely disappeared, although they later appeared at parietal sites.
Lacoste-Badie & Droulers, 2014	One hundred thirty under- and postgraduate students were recruited (60% women), ranging in age from 19 to 28 years	130	Recall and recognition (except for brand recognition), was significantly higher in the "grasping and drinking" condition than in the "no inter-action" condition.
Haker et al, 2013	Eleven right-handed healthy adults (five male, six females; 21–55 years old, mean age 31.5) volunteered for this study	11	The subjects indicated a mean conscious contagion in 55 % of the six yawning video sequences (SD = 30, min = 33 %, max = 100 %). Contagiousness was balanced, with no stimulus being significantly more contagious than another.
Kraskov et al, 2014	Three purpose-bred adult macaques (two males, M41 and M47, one female M43)	3	PTNs in area F5 evoked by action observation and potential transmitted to the spinal cord may be part of an "extended" mirror neuron system.

6. Conclusion:

Creutzfeldt – Jakob Disease is a completely fatal progressive cognitive decline related disease that has been around for decades and has affected individuals across the globe. Due to the nature of CJD and the current lack of understanding of the neurological structures and related pathways, potential treatments or even methods to prolong the course of the disease are non-existent. It has been assumed that once an individual is diagnosed with CJD there is no longer anything that can be done, and as such research into the potential pathways and specific groups of neurons that may be causing the observed symptoms, aside from complete brain neuronal failure after prion infection, is limited. Based on some of this research, however, a link between the characteristic symptoms of CJD and the Mirror Neuron system, independently, has been noted. Issues with Muscular coordination, Dementia, Personality changes, including impaired memory, judgment, and thinking, Depression and Movement Disorders including jerky limb movements, random muscle twitching, stiffness, inability to perform controlled movements, and dysarthria can be seen to each individually contain certain specific relationships to the Mirror Neuron System and be affected by it either positively or negatively. Although extensive research must be done on the subject and current medical technology/understanding may not be enough, the symptoms of CJD and the Mirror Neuron system may be related, dependently, and further insight may provide the basis for eventual treatment.

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