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The Networks of Neuropsychiatric Symptoms of Dementia and the Informal Caregiver in a House Setting

Project: A network approach to neuropsychiatric symptom dynamics in persons with dementia

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The Networks of Neuropsychiatric Symptoms of Dementia and the Informal Caregiver in a House Setting

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Introduction: Why At All Study the Neuropsychiatric Symptoms of Dementia from the Network Perspective

Watching a loved one's cognitive abilities decay, not because they are getting older but because of their dementia, is a difficult experience; especially when that person is the parent who brought you into this world. Dementia is a neurodegenerative disease that derogates the neurological functions by impairing or destroying the neurons in the brain. National Institute of Aging describes dementia as "the loss of cognitive functioning – thinking, remembering and reasoning – to such an extent that it interferes with a person's daily life and activities" (2022). Dementia becomes more prevalent (Kang et al., 2003) as people grow old, hence they require another person to take care of their basic needs as they themselves lose their ability to do so. These needs include but are not limited to running daily errands, cooking, dressing up, expression of thoughts, financial responsibility and physical balance along with the pain the patients with dementia experience physically or mentally, which is reported as the most burdensome part of having dementia by the patients. Their needs increase proportionally as the severity of dementia increases, and the patient with dementia grows a need for a person to live with them to fulfill their needs.

The person who is going to move in with the patient, we call the informal caregiver. An informal caregiver is generally a daughter, son or some other person in the family. Dementia is exhaustive, and the treatment process demands responsibility and cautiousness of the informal caregiver. Following, the loss of cognitive function the patient with dementia also experiences neuropsychiatric symptoms, which can make the person apathetic, hyperactive, arrogant, depressed, delusional, agitated, euphoric, irritated, insomniac, anorexic and the likes (for example, see delusion of theft of a patient with dementia: Ishimaru et al., 2022). The informal caregiver also experiences distress and agitation as the developments of these symptoms negatively impact the caregiver's psychological and mental wellbeing (Borsje et al., 2016). Borsje and colleagues report a stable pattern of psychological distress as the severity of dementia advances sequentially.

Neuropsychiatric symptoms change over time (Eikelboom et al., 2022) and it is difficult to predict the expected changes. As the informal caregiver is in proximity with the patient with dementia frequently, the caregiver experiences these neuropsychiatric symptoms and interacts with them without knowing.

Neuropsychiatric symptoms interact within themselves and the environment, which makes these symptoms a complex system of variables with parameters we lack the understanding of. In the environment, however, it is not only the surroundings but the caregiver the patient constantly is in interaction and in communication with. Thus, there is a regular back and forth between the patient with dementia and the informal caregiver in the house setting, which lays the foundation for our project as we suggest the caregiver burden is not the only network or variable the neuropsychiatric symptoms are interacting with, but rather the whole entity of the informal caregiver, a person, whom it is commonly asked to assess the neuropsychiatric symptoms of the dementia patients they are taking care of, using the Caregiver-Administered Neuropsychiatric Inventory (CGA-NPI) (Kang et al., 2022).

Table 1. Prevalence, Subscale Scores, and Correlation of Behaviors Rated by the Neuropsychiatric Inventory (NPI) and the Caregiver-Administered NPI (CGA-NPI)

Behavior	Prevalence (%)			Frequency (Mean[SD])			Severity (Mean[SD])			Distress of Caregiver (Mean[SD])		
	CGA-NPI	NPI	κ^a	CGA-NPI	NPI	r^b	CGA-NPI	NPI	r	CGA-NPI	NPI	r
Delusions	22 (36.1)	20 (32.8)	0.71	0.9 (1.4)	0.9 (1.4)	0.72	0.6 (1.0)	0.6 (1.0)	0.70	0.9 (1.6)	0.8 (1.4)	0.74
Hallucinations	15 (24.6)	10 (16.4)	0.75	0.6 (1.3)	0.5 (1.2)	0.80	0.4 (0.8)	0.3 (0.8)	0.76	0.7 (1.4)	0.4 (1.2)	0.81
Agitation	31 (50.8)	22 (36.1)	0.57	1.1 (1.3)	0.8 (1.3)	0.64	0.6 (0.7)	0.6 (1.0)	0.69	1.2 (1.7)	0.9 (1.5)	0.72
Depression	27 (44.3)	23 (37.7)	0.66	0.9 (1.2)	0.8 (1.2)	0.62	0.6 (0.8)	0.5 (0.8)	0.63	0.8 (1.3)	0.7 (1.1)	0.71
Anxiety	21 (34.4)	19 (31.1)	0.62	0.7 (1.2)	0.8 (1.4)	0.69	0.4 (0.7)	0.5 (0.8)	0.64	0.7 (1.3)	0.7 (1.3)	0.61
Euphoria	15 (24.6)	13 (21.3)	0.63	0.5 (1.1)	0.5 (1.2)	0.65	0.3 (0.8)	0.3 (0.8)	0.63	0.3 (1.1)	0.4 (1.1)	0.74
Apathy	34 (55.7)	31 (50.8)	0.57	1.3 (1.5)	1.9 (1.9)	0.58	0.8 (0.9)	0.9 (1.0)	0.68	1.2 (1.6)	1.1 (1.6)	0.60
Disinhibition	19 (31.1)	13 (21.3)	0.74	0.6 (1.2)	0.5 (1.2)	0.75	0.4 (0.8)	0.3 (0.8)	0.77	0.6 (1.5)	0.4 (1.3)	0.83
Irritability	23 (37.7)	27 (44.3)	0.79	0.9 (1.3)	1.0 (1.4)	0.74	0.6 (0.8)	0.7 (0.9)	0.77	1.1 (1.6)	1.1 (1.5)	0.76
Aberrant motor behavior	20 (32.8)	22 (36.1)	0.71	1.0 (1.5)	1.0 (1.6)	0.73	0.7 (1.0)	0.7 (1.1)	0.69	0.8 (1.4)	0.7 (1.3)	0.61
Nighttime behavior	12 (19.7)	19 (31.1)	0.61	0.8 (1.3)	0.5 (1.2)	0.70	0.4 (0.8)	0.3 (0.8)	0.60	0.7 (1.3)	0.6 (1.3)	0.73
Eating change	12 (19.7)	14 (23.0)	0.90	0.7 (1.4)	0.7 (1.6)	0.89	0.4 (0.8)	0.4 (1.0)	0.84	0.5 (1.1)	0.5 (1.3)	0.81
Total				0.8 (0.8)	0.8 (0.8)	0.84	0.5 (0.6)	0.5 (0.6)	0.88	0.8 (1.0)	0.7 (0.9)	0.86

a. Kappa value.

b. Spearman correlation.

(Kang et al., 2022)

Caregiver profile has been widely studied in the Geriatrics literature, because it influences the progression of the dementing disorder, hence the reason we have chosen to characterize the caregiver as a network of 3 continuous and 3 categorical parameters. Both the neuropsychiatric symptoms of dementia and the informal caregiver have not been studied as networks prior to our project.

The most common technique or approach in medicine to diagnose a disease is based on detecting its symptoms which sustain longer than a certain period of time and cause distress (i.e., physical pain) for the person.

Network approach, in the meantime, has been becoming more and more widely used and depended on, especially in psychological studies, and what inspired this project in applying to network perspective was also a psychological study based on establishing Major Depression Disorder (MDD) as a “complex dynamic system” (Cramer et al., 2016). A complex dynamic system characterizes symptoms with consideration of their interactions and connections into one another with other variables (e.g., other symptoms) from a network infrastructure. This network infrastructure, when applied to symptoms, helps establish stronger and weaker bonds called as “edges”. These edges in response indicate “vulnerabilities” of the system or individual. Cramer and colleagues showed that however strong these bonds were, the patient or person was more inclined to develop depression. Cramer and colleagues suggest that applying the network approach can improve the applications of intervention, and proposed they were the first to suggest the first symptom based process model of depression.

Building upon their findings, we wanted to test how we could apply this approach to medicine. Specifically, the progression of dementia. Unless the symptoms are apparent, dementia is very difficult to diagnose in the early stages, which leads to a burdening treatment process for the patient with dementia. Neuropsychiatric symptoms similarly appear in the later stages which again toughens the process of early detection, and even so when they appear they can counter the positive effects of treatment (Lyketsos et al., 2002; Steffens et al., 2005), which makes it even more critical to recognize the interaction between these symptoms to achieve early diagnosis and less burden for both sides. In agreement with this, studies show that patients with dementia get misdiagnosed with psychological disorders (i.e., depression, anxiety) (Aalten et. al.,

2017), which again strengthens our motive to propose this infrastructure to study the neuropsychiatric symptoms of dementia.

The patient is not the only affected party in this sequence of treatment as they are generally accompanied by a close relative, family member or a friend, which creates a burden upon their psychological wellbeing. Experiencing dementia, both for the patient and the informal caregiver, is an exhaustive process, hence considering this, we also believe the caregiver should be examined from the network perspective. For this, we propose 2 different options: (i) considering the caregiver burden as a network and (ii) characterizing the informal caregiver by 6 variables and recognizing the interaction with those variables and the neuropsychiatric symptoms of the patient with dementia. We discuss those variables in depth in the later sections. In conclusion, we expect those interactions to influence the psychological wellbeing of the informal caregiver and the progression of dementia for the patient with dementia. Our main objective in doing this relies upon encouraging the medical literature to recognize the interplay between the neuropsychiatric symptomal network and its subsyndromal effects with the informal caregiver network as the foreword of dementia to build a symptomal network modelling perspective that visualizes these relations. We repeatedly point out the strong influence of the informal caregiver on the course of the development of the neuropsychiatric symptoms. We now outline the neuropsychiatric symptoms of dementia.

1. Neuropsychiatric Symptoms of Dementia

Neuropsychiatric symptoms (NPS) are the symptoms of dementia that are also within psychological roots, lead to divergences from the everyday life behavior and attitude of the patient, rarely present in the beginning of the disease and often seen as dementia progresses into moderate stages, characterized as mood, psychotic, and frontal types, and any of them is seldom observed in isolation. Neuropsychiatric symptoms emerge as the severity of the dementia increases and are prevalent in dementia (Linde et al., 2018).

Building up on the meta-analysis and systematic review of Zhao et al. we limit the boundaries of the project to the 12 symptoms of the Neuropsychiatric Inventory (NPI) (Zhao et al., 2015). We list these 12 neuropsychiatric symptoms below, with their respective example(s) for the symptoms that are not as commonly known.

1.1. 12 Neuropsychiatric Symptoms: Neuropsychiatric Inventory (NPI) (Cummings et al., 1994)

1. Delusions

False belief, abnormal thought content.

Example. Suspiciousness, abandonment, misidentification

2. Hallucinations

Sensory perception in absence of sensory stimuli.

Example. Well formed images/animals with explicit details

3. Agitation / Aggression

Inappropriate verbal, vocal, motor activity.

Examples. Wandering away from home, Repetitive/purposeless behaviors

4. Depression / Dysphoria

Characterized by rapid emotional shifts.

Examples. Anhedonia, Sadness, Hopelessness, Loss of self-esteem, expression of somatic concern, tension, panic.

5. Anxiety

Predictor of allocation of the patient with dementia to nursing home.

Associated with poor quality of life, behavior problems, impairment of activities of daily living, sleep disturbances and poorer cognitive functions.

Examples. Less coping ability in daily living, loss of control, fear for the future (Kwak et al., 2017).

6. Euphoria / Elation

Pre-dementia syndrome.

Examples. Mania, elation.

7. Apathy / Indifference

Loss of motivation.

Examples. Reduced emotional expression, low vitality, poor initiative, and diminished goal-directed behavior (Yeager et al., 2008).

8. Disinhibition

Socially disruptive or morally unacceptable behaviors.

(Magrath Guimet et al., 2021)

Examples. Loss of manners, impulsiveness.

9. Irritability/Lability

Neurobehavioral symptom and a predictor of more rapid decline.

(Ismail et al., 2018)

Example. Mood disorder.

10. Aberrant Motor

- a. Motor Retardation: slowed movements, speech, reduced body tone and less spontaneous body movements
- b. Motor Hyperactivity: increased energy level, more frequent movements, rapid speech

11. Nighttime Behavior

Disturbances in Circadian Rhythm.

Examples. Hypersomnia, Insomnia, sleep-wake cycle reversal, fragmented sleep, rapid eye movement sleep behavior disorder, nighttime awakening.

12. Appetite

a. Anorexia/hyperphagia

Patients with dementia lose weight due to hypermetabolism and inflammatory processes.

Food Preference

b. Qualitative/quantitative preference for particular foods

Example. preference for sweets

For a review of these symptoms, see Cerejeira et al., 2012, Ismail et al., 2018)

2. Linking Neuropsychiatric Symptoms of Dementia to Networks (Complexity Science)

We have briefly mentioned the importance of networks in the introduction, however we have not touched upon the complexity science relation of networks. To be more precise, complex is used to mean “having many parts related to each other in ways that may be difficult to understand” (Cambridge Dictionary), and complex systems are considered as the study of non-linear, chaotic complex systems that are difficult to predict. Complexity science requires a dynamic system based on the interplay between 2 or more variables and how they constantly and unpredictably interact within each other and their environment, which we refer to as network interaction. Radboud Interfaculty Complexity Hub (RICH) similarly identifies complex systems as “emergent, non-linear and dynamical, and unpredictable” (RICH, “What is complexity science?”, 2021) Complexity science argues systems will rarely be found in isolation of other variables. Hence, studying isolated systems will derogate ecological validity of the results and will not be fully applicable to solve complex problems of the modern world. Health and clinical care literature converges upon this result (e.g., Plsek et al, 2001; Wilson et al., 2001), as biological systems are composed of intrinsically complex and interconnected mechanisms. Moreover these neuropsychiatric symptoms themselves also “fluctuate” over time (Eikelboom et al., 2022) as we have pointed out in the interaction.

2.1. Importance of Studying Diseases as Network Interactions in Medicine

As we have pointed out, our biological systems are made of complex mechanisms that are difficult to predict, which the medical literature converges on. Yet this does not explain why we should study diseases or disorders as network interactions. Up until now, diseases would be understood and diagnosed from the Common View approach, which we now understand failed to reflect upon the inner workings of complex systems, since it neglected the interaction between the symptoms.

2.2. Common View Approach in Medicine

A disease causes symptoms to emerge and by observing those symptoms, the disease is diagnosed by medical experts, this is the disease model as commonly practiced in medicine. See a figure of a psychological disorder, major depression (MD), based on the disease model below.

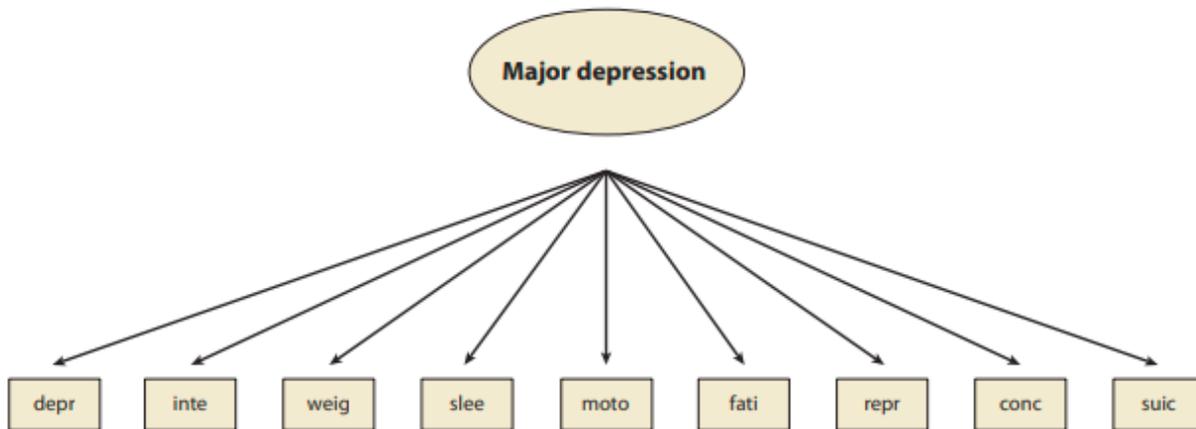


Figure 1

The relation between the disorder major depression (MD) and its observable symptoms according to a medical disease model. According to this model, MD (the oval at the top of the figure) is the root cause of its observable symptoms (the boxes at the bottom of the figure). Arrows point from the root cause (MD) to its observable symptoms, but not the other way around. See **Table 1** for definitions of abbreviated terms.

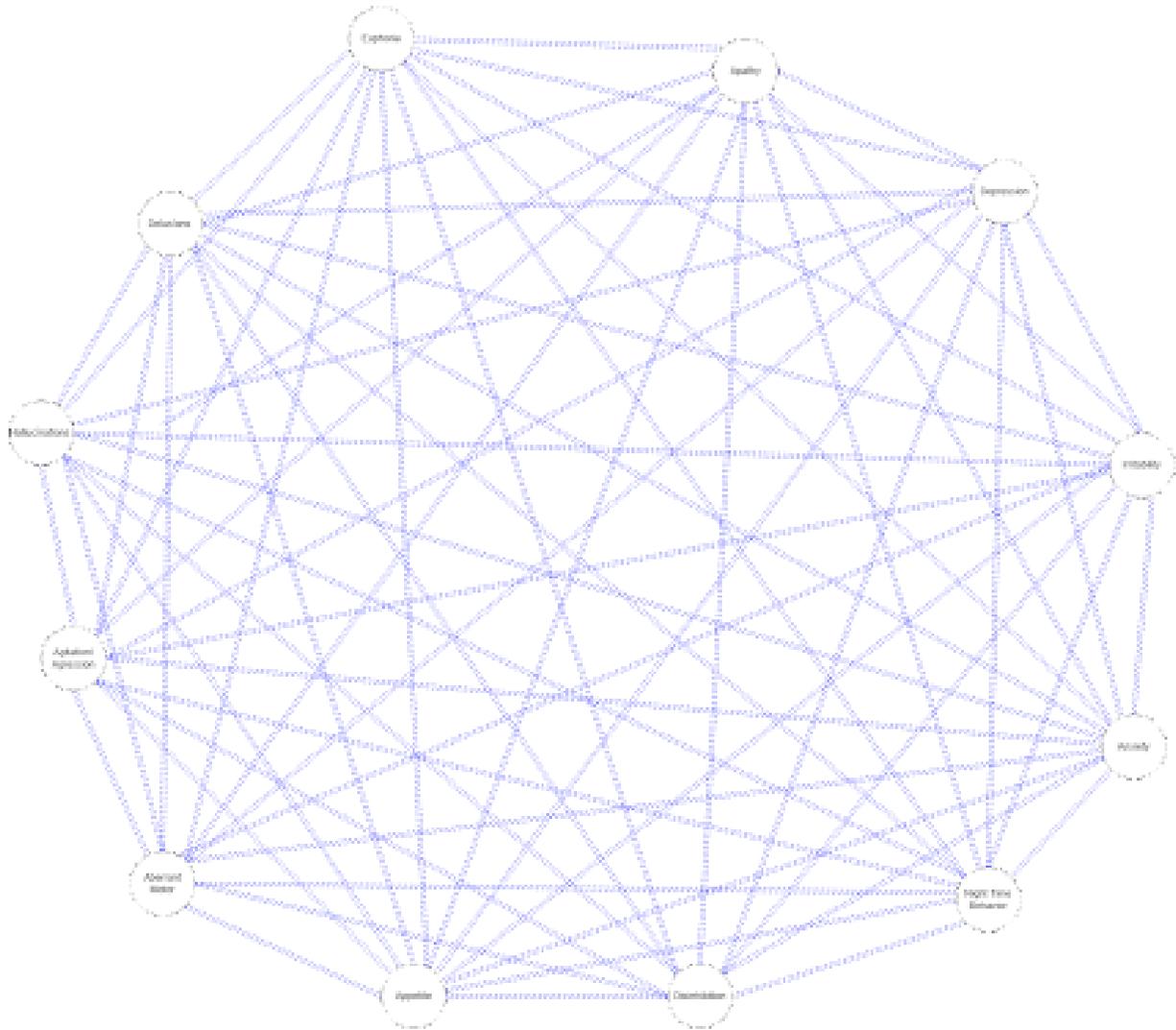
(Borsboom and Cramer, 2013)

As the figure illustrates, the psychological disorder leads to the emergence of symptoms and these symptoms are portrayed as disconnected, like there is not any interaction between these symptoms that impact the progression of the disease.

However, as the studies show us, the common view approach is not enough as the symptoms are not isolated from each other, the symptoms create networks, and they interact with each other over time. This leads to alterations in the expected progression of the disease, thereby increasing its negative influence on both the patient with dementia and the informal caregiver.

2.3. Neuropsychiatric Symptom Network Modeling Example

There are numerous options to visualize the network we have been discussing so far. It is of importance to note down a few even if they require more work to portray an accurate model of their interaction with the caregiver network. It also matters to mention that while considering this, we have disregarded the factor of environment. The future studies, for instance, could focus on the environmental characteristics of the house the patient with dementia is living in by setting specific parameters.



Neuropsychiatric Symptom Network Modeling Example

Based on the aforementioned 12 neuropsychiatric symptoms.

3. House Setting

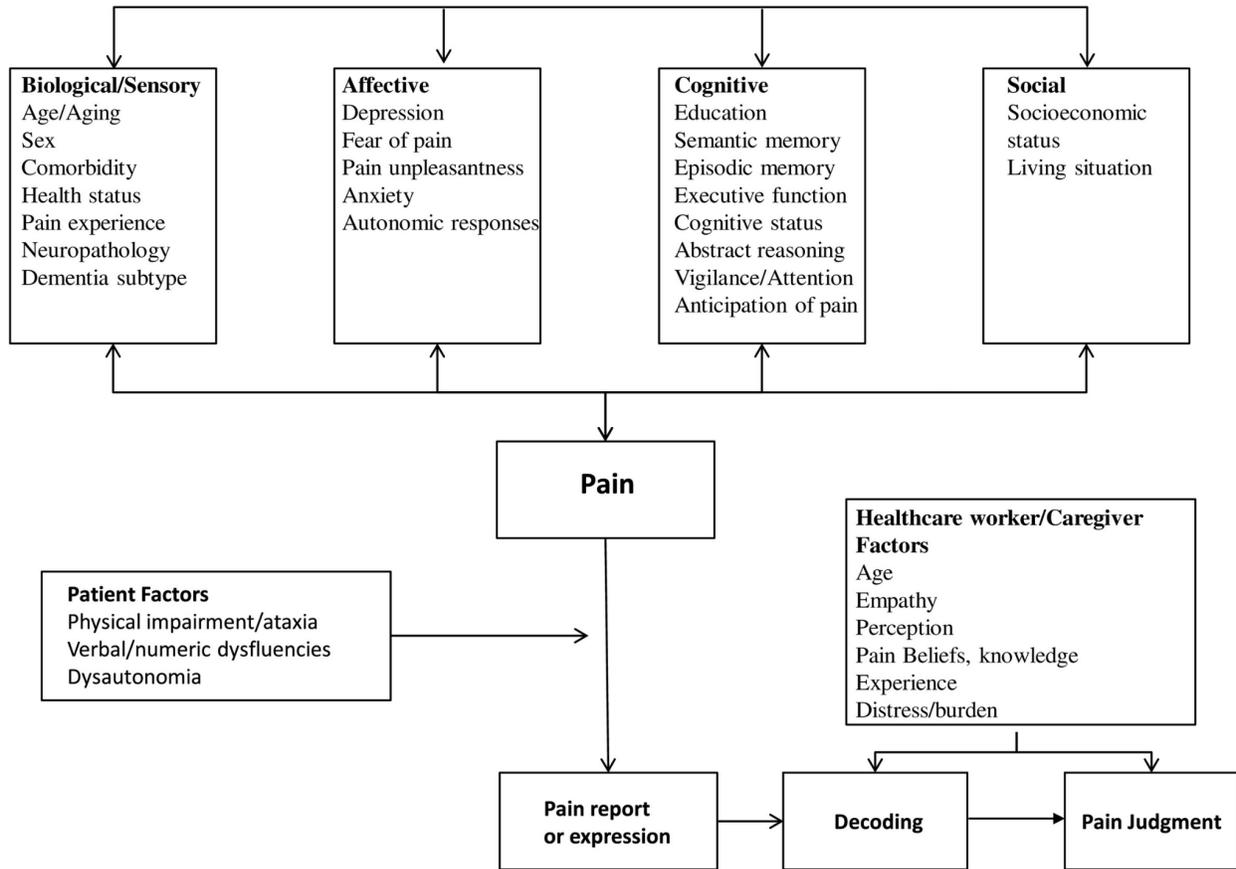
Although in the Dutch medicine literature studies are more prevalent in nursing homes, we believe and emphasize in our project that it is highly common for the patients with dementia in the Netherlands to be taken care of by an informal caregiver in the patients' own houses. This simply means that other than necessary medical check ins, the patient still maintains their basic functionalities. We discuss who this caregiver can be in the upcoming section.

Why this study matters is because the Dutch medicine literature has so far focused on the nursing homes, this could be because it was accessible, obtaining permission from the patient to conduct a study in their houses may lead to a conflict, especially if the interaction between the informal caregiver and the patient with dementia has a derogating effect on the disease (Gagliese et al., 2018).

4. Informal Caregiver

Informal caregiver, from running daily errands on behalf of them to helping patients with dementia respond to basic hygiene needs and nutrition (i.e., healthy diet), helps the patient maintain their daily activities and fundamental human needs. This person can be someone from the family, or a close friend. In the Netherlands, the majority of these people are either daughters and sons, they are taking care of a family member who is diagnosed with dementia and experiencing to cope with their neuropsychiatric symptoms. This is very difficult and challenges the resilience of the caregivers frequently because these symptoms interact within each other and the environment. What stimuli could trigger the resilience of the informal caregiver is also quite difficult to estimate. Resilience is relative, but can be trained. Nonetheless, resilience is not the only factor that causes this interplay between the caregiver and patient with dementia. We categorize these variables more explicitly in section 5.

What inspired this categorization was the proposal of a biopsychosocial model of pain and dementia, which characterizes the caregiver under 6 categories (see below): age, empathy, perception, pain beliefs or knowledge, experience, distress or burden (Gagliese et al., 2017; Melzack and Katz, 2013; Prkachin et al., 2007; Spector and Orrell, 2010).



“Healthcare Worker / Caregiver Factors”

(Gagliese et al., 2017; Melzack and Katz, 2013; Prkachin et al., 2007; Spector and Orrell, 2010)

Further to this, Kerpershoek and colleagues have identified “caregiver profiles” that we believe support this concept of examining the caregiver as a network of different parameters and variables (Kerpershoek et al., 2018). We have similarly recognized two ways of addressing the caregiver as a network: caregiver burden and caregiver itself as a network of 6 parameters. We discuss this later in the upcoming section.

5. Caregiver Burden Network

What makes this project influential is the mere fact that networks are not static entities. Further to a network interacting with its own nodes, a network and variables of a network can interact with other networks (Kalisch et al., 2019). In this case, we expect a communication between the neuropsychiatric symptoms of dementia and the network of a caregiver. We especially expect the interaction to be significant because as we have formerly mentioned, we identified 6 different parameters to characterize the informal caregiver, one of them being the importance of the sex of the caregiver. Eikelboom and colleagues, for example, found that female informal caregivers are more likely to experience severe psychological distress (Eikelboom et al., 2022).

Fischer and colleagues (Fischer et al., 2012) have reviewed the medicine literature and found 14 papers that focused on the burdens of caregivers, a clear link between neuropsychiatric symptoms of dementia and impact of caregivers, and they have suggested interventions, both pharmacological and non-pharmacological types, must be based on the managing NPS. We consider this by applying their findings into 2 different frameworks to construct the informal caregiver as a network in addition to our modeling of neuropsychiatric symptom networks.

6. Neuropsychiatric Symptoms and Informal Caregiver Networks Modeling

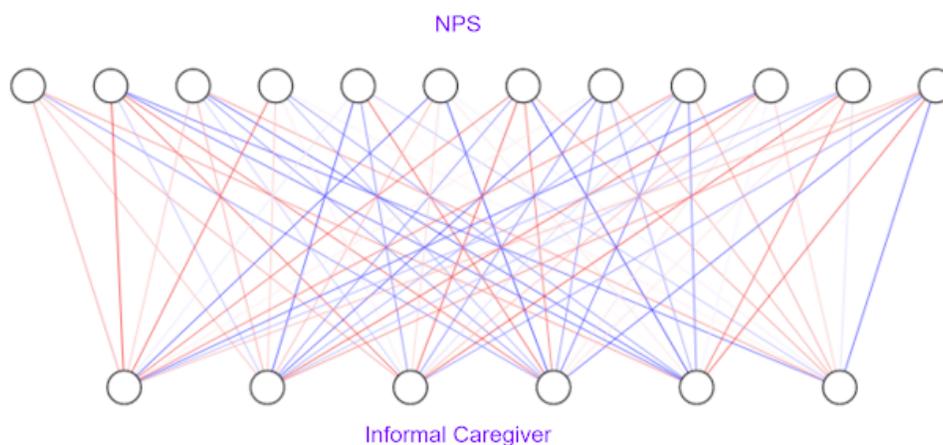
Exact prediction of the interaction of all 12 of the NPS with their connection to the 6-variable network of our caregiver will be nearly impossible in our current circumstances, however we still prefer to present the idea as a whole as a reference to future studies in the symptom network approach.

There are various ways of characterizing this interaction, yet before we explain the models, we would like to justify the reasons for having visualized this figure with this outlook.

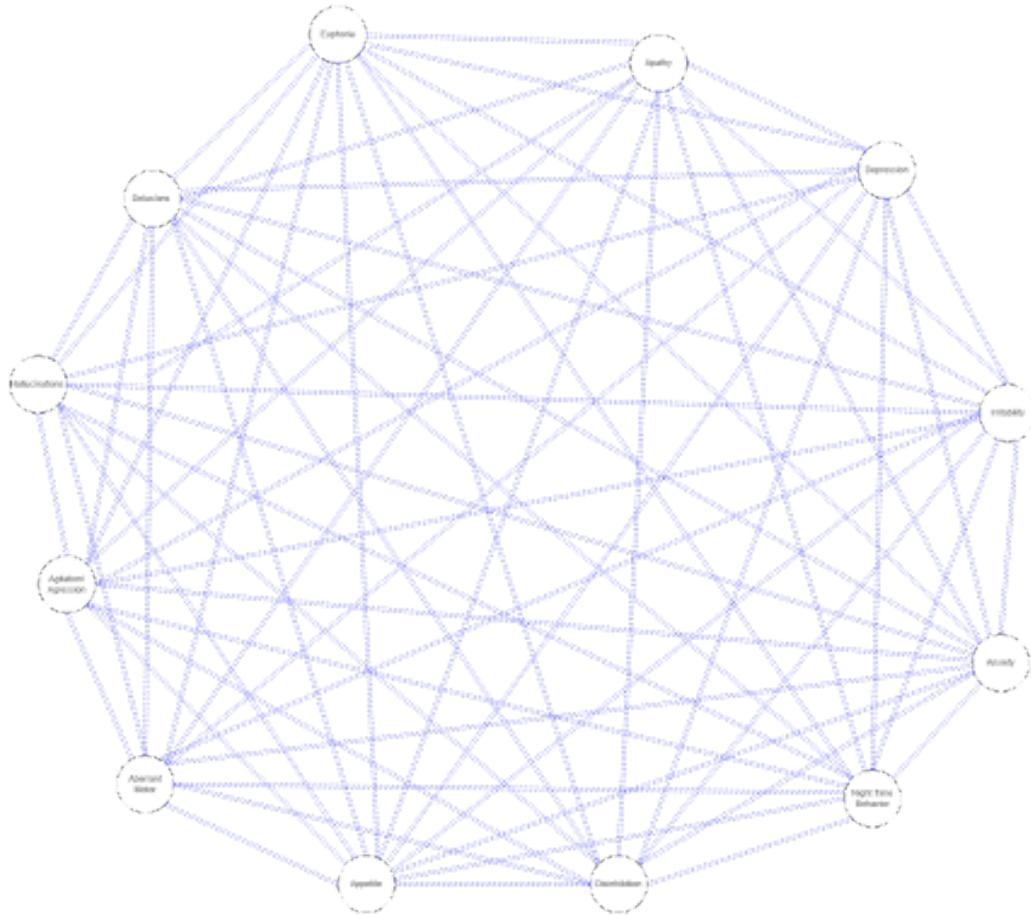
First, we have started with the classic modeling technique of network methodology (i.e., nodes and edges) and applied the technique to visualize the features of the interaction of the neuropsychiatric symptoms and the informal caregiver networks.

Second, since we know that these interactions happen in a house setting, we have considered an “inside out” interaction, suggesting that these two networks behave as one during the time of their interaction.

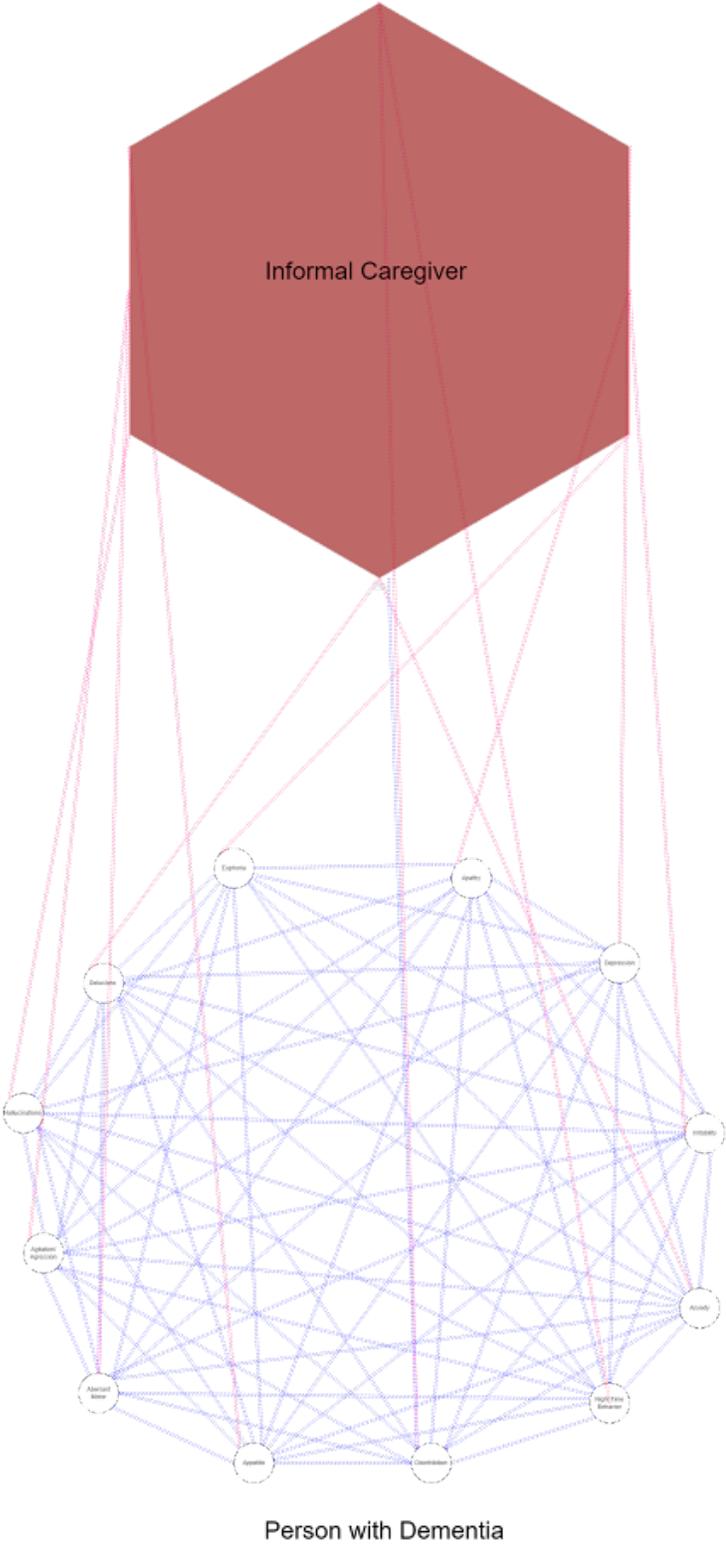
Third, we have characterized the caregiver as a network with one variable, as the caregiver burden we have discussed.



Neuropsychiatric Symptoms and the Informal Caregiver Networks Modeling Example 1



Neuropsychiatric Symptoms and the Informal Caregiver Networks Modeling Example 2



Neuropsychiatric Symptoms and the Informal Caregiver Networks Modeling Example 3

7. Future Suggestions

We should emphasize what we are proposing here visually is algebraically very difficult to accurately estimate and this is an important limitation of this project. In order for this model to work, real-time data should be collected and regularly fed into the system using machine learning and artificial intelligence, which we have initially intended but could not carry out in this project. Considering the environment by identifying certain environmental parameters that could influence the disease as a network can also help clarify if the environment has a significant impact on the interactive model we have proposed between the neuropsychiatric symptoms of dementia and the informal caregiver networks. Future studies may also consider the framework we have outlined as a predictor of the progression of dementia, and base their introspective methods on the parameters we have identified. We additionally encourage a mathematical study to construct a mathematical model for the framework we have figuratively outlined as that was a limitation we have encountered during our research.

8. References

Fischer CE, Ismail Z, Schweizer TA. Impact of neuropsychiatric symptoms on caregiver burden in patients with Alzheimer's disease. *Neurodegener Dis Manag.* 2012;2: 269–277

Cramer AOJ, van Borkulo CD, Giltay EJ, van der Maas HLJ, Kendler KS, Scheffer M, et al. (2016) Major Depression as a Complex Dynamic System. *PLoS ONE* 11(12): e0167490. doi:10.1371/journal.pone.0167490

Radboud-complexity.com. 2022. [online] Available at: <<https://www.radboud-complexity.com/complexity-science>> [Accessed 13 October 2022].

Plsek, P. E., & Greenhalgh, T. (2001). Complexity science: The challenge of complexity in health care. *BMJ (Clinical research ed.)*, 323(7313), 625–628.

<https://doi.org/10.1136/bmj.323.7313.625>

Wilson, T., Holt, T., & Greenhalgh, T. (2001). Complexity science: complexity and clinical care. *BMJ (Clinical research ed.)*, 323(7314), 685–688.

<https://doi.org/10.1136/bmj.323.7314.685>

Cerejeira J, Lagarto L and Mukaetova-Ladinska EB (2012) Behavioral and psychological symptoms of dementia. *Front. Neur.* 3:73. <https://doi.org/10.3389/fneur.2012.00073>

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*, 44(12), 2308-2308.

Eikelboom, WS, den Teuling, A, Pol, DE, et al. Biweekly fluctuations of neuropsychiatric symptoms according to the Neuropsychiatric Inventory: erratic symptoms or scores? *Int J Geriatr Psychiatry.* 2022; 1- 7. <https://doi.org/10.1002/gps.5770>

Kerpershoek, L., Woods, B., Wolfs, C., Verhey, F., Jelley, H., Bieber, A., Stephan, A., Michelet, M., Selbaek, G., Handels, R., Wimo, A., Hopper, L., Irving, K., Marques, M. J., Gonçalves-Pereira, M., Portolani, E., Zanetti, O., de Vugt, M., & Actifcare Consortium (2020). Do caregiver profiles predict the use of dementia care services? Findings from

the Actifcare study. *Aging & mental health*, 24(2), 272–279.

<https://doi.org/10.1080/13607863.2018.1544215>

Kang, S. J., Choi, S. H., Lee, B. H., Jeong, Y., Hahm, D. S., Han, I. W., ... Na, D. L. (2004). *Caregiver-Administered Neuropsychiatric Inventory (CGA-NPI)*. *Journal of Geriatric Psychiatry and Neurology*, 17(1), 32–35. doi:10.1177/089198873258818

Ishimaru D, Kanemoto H, Hotta M, Nagata Y, Satake Y, Taomoto D and Ikeda M (2022) Case Report: Treatment of Delusions of Theft Based on the Assessment of Photos of Patients' Homes. *Front. Psychiatry* 13:825710. doi: 10.3389/fpsy.2022.825710

Borsje, P., Hems, M. A., Lucassen, P. L., Bor, H., Koopmans, R. T., & Pot, A. M. (2016). Psychological distress in informal caregivers of patients with dementia in primary care: course and determinants. *Family practice*, 33(4), 374–381.

<https://doi.org/10.1093/fampra/cmw009>

Kalisch, R., Cramer, A. O. J., Binder, H., Fritz, J., Leertouwer, Ij., Lunansky, G., Meyer, B., Timmer, J., Veer, I. M., & van Harmelen, A.-L. (2019). Deconstructing and Reconstructing Resilience: A Dynamic Network Approach. *Perspectives on Psychological Science*, 14(5), 765–777. <https://doi.org/10.1177/1745691619855637>

Gagliese, Lucia; Gauthier, Lynn R.; Narain, Nadine; Freedman, Tamlyn (2017). *Pain, aging and dementia: Towards a biopsychosocial model*. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, (), S0278584617303834–. doi:10.1016/j.pnpbp.2017.09.022

Van der Linde, R., Dening, T., Stephan, B., Prina, A., Evans, E., & Brayne, C. (2016). Longitudinal course of behavioural and psychological symptoms of dementia: Systematic review. *British Journal of Psychiatry*, 209(5), 366-377. doi:10.1192/bjp.bp.114.148403

Kwak, Y. T., Yang, Y., & Koo, M. S. (2017). Anxiety in dementia. *Dementia and neurocognitive disorders*, 16(2), 33.

Ismail, Z., Gatchel, J., Bateman, D. R., Barcelos-Ferreira, R., Cantillon, M., Jaeger, J., ... & Mortby, M. E. (2018). Affective and emotional dysregulation as pre-dementia risk

markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. *International psychogeriatrics*, 30(2), 185-196.

Yeager, C. A., & Hyer, L. E. E. (2008). Apathy in dementia: relations with depression, functional competence, and quality of life. *Psychological reports*, 102(3), 718-722.

Magrath Guimet, N., Miller, B. L., Allegri, R. F., & Rankin, K. P. (2021). What do we mean by behavioral disinhibition in frontotemporal dementia?. *Frontiers in Neurology*, 12, 707799.

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