Identification of predictive factors for neuropsychiatric symptoms across neurodegenerative disorders: Baseline results of a longitudinal study

Owen Skoda, B.Sc., M.Sc.(c)[1,2,3], Danika Rioux, B.Sc.[1,2,3], Clara Vo-Dignard, B.Sc.[1,2,3], Philippe Desmarais, M.D., FRCPC, M.H.Sc.[1,2,3]

1. Centre Hospitalier de l'Université de Montréal (CHUM), Québec, Canada; 2. Département de Neurosciences, Faculté de Médecine, Université de Montréal, Québec, Canada;
3. Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), Québec, Canada

BACKGROUND

- **Neuropsychiatric symptoms (NPS) in neurodegenerative and neurocognitive disorders** present in up to 97% of individuals over a 5-year period and are a major contributing factor to the socio-economic costs (Kapustin et al., 2023).
- **NPS are clinically heterogeneous**, with major variability in presentations and prognoses (Cerejeira et al., 2012).
- **Incidence of NPS is affected by multiple factors,** for example caregiver burden and cerebral vascular changes (Pinyopornpanish et al., 2021).
- While it is known that specific NPS can predict trajectories and emergence of other NPS, **overall prediction of NPS trajectories over time remains a challenge** (Prado-Jean et al., 2010).
- **Identification of predictive factors** for emergence and persistence of NPS across neurodegenerative disorders **would have critical clinical utility.**

OBJECTIVE

- **Characterize NPS features** across neurodegenerative disorders (i.e., Alzheimer's disease [AD], Lewy body dementia [LBD], and Frontotemporal dementia [FTD]) and **identify potential predictive factors of NPS**, such as underlying neuropathological processes.

CONCLUSION

- Our data show **differences in the presentation of NPS** between different neurodegenerative disorder diagnoses
- Our data also show **multiple potential predictive factors of NPS** across neurodegenerative disorder diagnoses.
- Although these results are far from being directly applicable in a clinical setting, they could **inform the development of tools used for earlier detection of potential NPS in medical care**
- Furthermore, they could also aid in raising **awareness of both risk factors and specific behaviours associated with NPS**

REFERENCES

1. *Kapustin D, Zarei S, Wang W, et al. Neuropsychiatric Symptom Burden across Neurodegenerative Disorders and its Association with Function. Can J Psychiatry. 2023;68(5):347-358. doi:10.1177/07067437221147443*
2. *Cerejeira, J., Lagarto, L., & Mukaetova-Ladinska, E. B. (2012). Behavioral and Psychological Symptoms of Dementia. Frontiers in Neurology, 3, 73. https://doi.org/10.3389/fneur.2012.00073*
3. *Pinyopornpanish, M., Pinyopornpanish, K., Soontornpun, A. et al. Perceived stress and depressive symptoms not neuropsychiatric symptoms predict caregiver burden in Alzheimer's disease: a cross-sectional study. BMC Geriatr 21, 180 (2021). https://doi.org/10.1186/s12877-021-02136-7*
4. *Prado-Jean, A., Couratier, P., Druet-Cabanac, M., Nubukpo, P., Bernard-Bourzeix, L., Thomas, P., Dechamps, N., Videaud, H., Dantoine, T., & Clément, J. P. (2010). Specific psychological and behavioral symptoms of depression in patients with dementia. International Journal of Geriatric Psychiatry, 25(10), 1065–1072. https://doi.org/10.1002/gps.2468*

METHODOLOGY & RESULTS

- **Design: Cross-sectional analysis of the baseline results of a longitudinal cohort study currently ongoing at the cognition clinic at the CHUM.**
- **Eligibility Criteria**:
  1. **Individuals diagnosed with a neurodegenerative disorder** (aged ≥60 years)
  2. **Associated caregivers** (capability of reporting NPS [at least 4 days a week])
- **Variables**:
  1. **NPS**: Measured using the **Neuropsychiatric Inventory (NPI)**, which measures 12 symptoms according to frequency (F) and severity (S), which are multiplied (FxS) to give an overall composite score of symptom intensity
  2. **Potential predictive factors**: Age, sex, clinical stage (Clinical Dementia Rating [CDR]), education, MMSE and MoCA, vascular risk factors, Zarit Burden Interview (ZBI)
- **Statistical Methods:**
  1. **Kruskal-Wallis test** were used to determine **group differences** in NPS according to the specific neurocognitive disorder
  2. **Ordinal Logistic Regressions** were used between potential predictive factors (baseline characteristics) and NPS (NPI composite score, NPI FxS)

Table 1. Demographic & Baseline data

	AD N = 68	LBD N = 20	FTD N = 11	TOTAL N = 99
AGE (mean, SD; in yrs)	81.7±6.9	79.5±6.3	77.0±8.1	80.6±7.0
SEX (%, F)	61.8	45.0	45.5	56.0
CDR (mean, SD)	1.6±0.8	0.9±0.5	0.9±0.4	1.4±0.7
MMSE (mean, SD; x/30pts)	20.1±5.9	23.2±8.4	21.5±9.6	20.7±6.7
MoCA (mean, SD; x/30pts)	18.4±3.5	20.8±4.0	18.2±4.5	19.3±4.0
ZBI (mean, SD; x/80pts)	30.4±14.1	31.5±16.3	38.3±21.3	31.4±15.4
PREVALENCE OF AT LEAST ONE CLINICALLY SIGNIFICANT NPS (%)	76.5	85.0	72.7	77.8
MOST PREVALENT NPS	APA (41.2%)	ANX (50.0%)	SD (54.5%)	APA (40.4%)

Abbreviations: APA: Apathy; H: Hallucinations; EX: Exaltation; ANX: Anxiety; SD: Sleep Disorder).
An NPS is deemed clinically significant if NPI FxS >3pts.

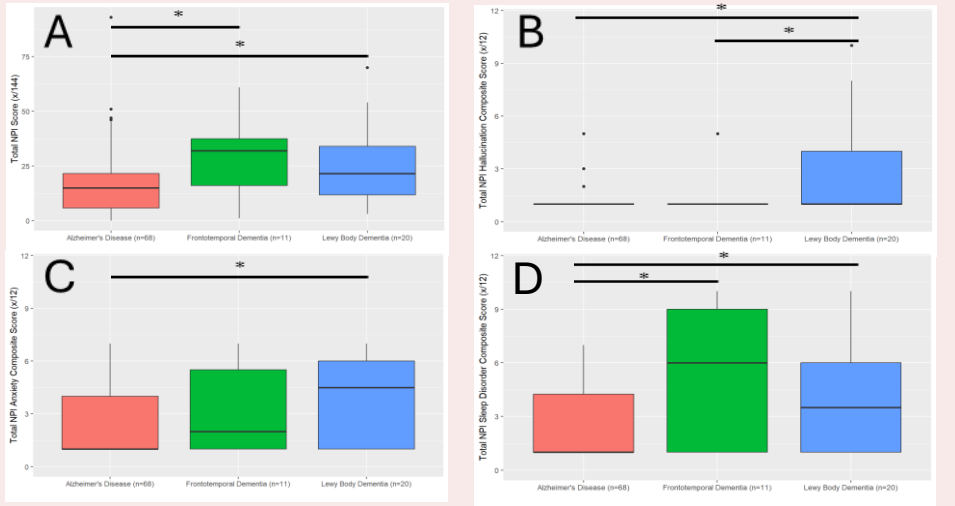

Figure 1. Boxplots of the distributions of total NPI score and FxS scores for symptoms with significant difference between diagnostic groups. **A.** Total NPI Score; **B.** Hallucinations; **C.** Anxiety; **D.** Sleep Disorder. (*: p<0.05)

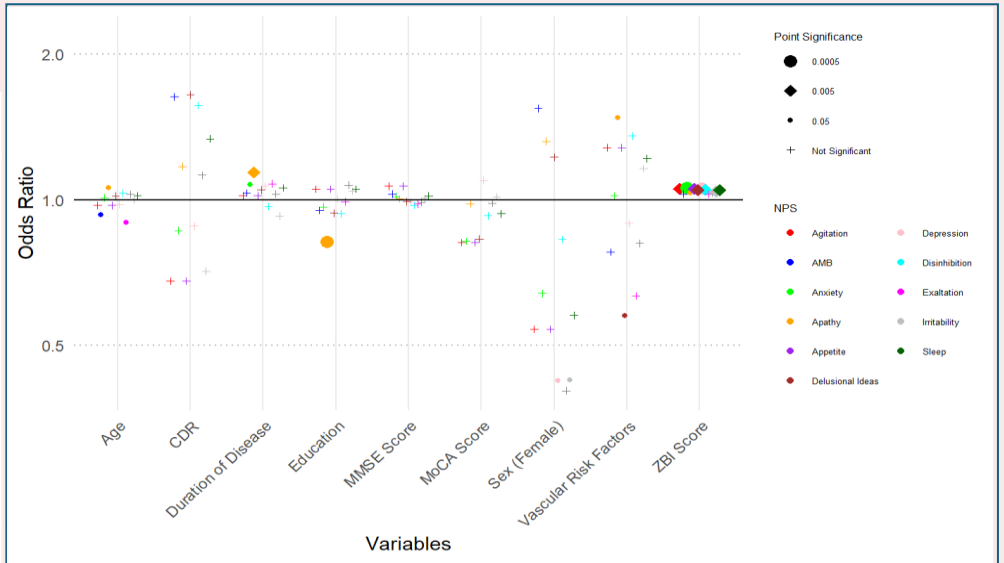

Figure 2. Scatterplot depicting the odds ratios of a specific symptom occurring depending on 9 different predictive factors (age, CDR score, duration of disease, education, MMSE & MoCA score, sex, vascular risk factors [i.e., arterial hypertension, diabetes, dyslipidemia, cardiovascular disease] and ZBI score) across neurodegenerative disorders. For example, older people are significantly more likely to suffer from apathy than their younger counterparts, however they are significantly less likely to suffer from either Aberrant Motor Behaviours (AMB) and exaltation