Associations between Brain Structure and Social/Occupational Function: A Secondary Analysis of the NIMH Intramural Dataset

Vincent Lee

Received August 29, 2024
Accepted December 17, 2024
Electronic access December 31, 2024

Social and occupational functions are essential components of overall well-being, and individuals with neuropsychiatric disorders often struggle with impaired social and occupational abilities. Research has consistently shown that specific brain networks, including those involved in social cognition, motivation, and cognitive control, play a critical role in regulating social and occupational functions. This study aimed to investigate the associations between brain structure and social and occupational function in a healthy adult population using the National Institute of Mental Health (NIMH) intramural dataset. The results showed significant volumetric differences in the pallidum between individuals with high and low social and occupational functioning, with females displaying larger effect sizes than males. These findings suggest that the pallidum may play a key role in social and occupational functioning and that sex differences may exist in the involvement of this region. This study highlights the importance of pallidum in future clinical implications for combating psychiatric illnesses and supports the potential of pallidum-targeted therapeutics for treating social and occupational dysfunction. This study also demonstrates the value of using open-source datasets, such as those from OpenNeuro, to test key hypotheses and advance the understanding of neuroimaging mechanisms underlying clinical phenotypes.

Keywords: Pallidum, social functioning, occupational functioning, MRI, NIMH intramural Dataset, brain structure, SOFAS

Introduction

Social and occupational functions are crucial to individual health. Social function describes an individual's ability to communicate and interact with other people. These include family, friends, teachers, co-workers, and strangers. Studies show that individuals with strong social functioning possess better cognitive ability, executive function, and longevity[1]. Occupational function is an individual's ability to fulfill tasks effectively and efficiently[2]. This encompasses home chores, homework, cleaning, and job duties. Good occupational function allows individuals to maintain proper hygiene and improves employee job satisfaction and job evaluation[3].

Patients with neuropsychiatric disorders often have impaired social and occupational functions. Studies found a significant correlation between social and occupational functions and age of onset and duration of illness in patients with schizophrenia[4]. Social and occupational dysfunctions have also been observed in patients with bipolar disorder. Their neurocognitive deficits, including executive functions and self-regulation, are associated with and predictive of diminished occupational functioning[5]. Furthermore, patients with Parkinson's disease have been found to have less expressive emotion and lower social functioning[6]. Patients with Alzheimer's disease have also shown decreased social function and ability to conduct self-care and daily activities[7].

Numerous studies have investigated how the brain may regulate social and occupational functions and how brain structural abnormalities may affect these functions. Large-scale meta-analyses on neuroimaging and human social interactions have identified key brain networks that are implicated in social cognition, motivation, and cognitive control, including default mode network, salience network, subcortical network, and central executive network[8]. Furthermore, it has been found that widespread brain changes are associated with social functioning in youth at clinically high risk for psychosis[9]. Additionally, a common neurophysiological basis of occupational neuroplasticity across different occupations has been identified[10]. Brain regions such as the anterior cingulate cortex[11], amygdala[12], and pallidum[13] have been frequently identified as key regions for reward, motivation, and social functioning. Collectively, these findings underscore the significance of understanding the neuroimaging mechanisms underlying social and occupational functions.

To accelerate scientific efforts to understand neuroimaging mechanisms underlying physiological and pathological processes and conditions, OpenNeuro[14], a BRAIN Initiative data archive, has been established to openly share data from a broad

© The National High School Journal of Science 2024

range of brain imaging data. More than 600 datasets are currently available on OpenNeuro, including a collection of comprehensive clinical assessments and neuroimaging data from healthy volunteers established by the NIMH[15]. Leveraging this rich dataset, this study aimed to investigate the associations between the structural differences in specific brain regions and social and occupational functions. We hypothesize that such specific brain regions may play a key role in these processes on the basis that past studies have shown that abnormalities and aberrations in brain volume, surface area, and other metrics correlate with altered social and occupational function[16]. To test this hypothesis, an unbiased analysis of subcortical regions was first conducted to compare participants with high and low social and occupational function, with gender included as a potential confounding factor and adjusted accordingly. Following the identification of significant brain regions, a secondary analysis was carried out to investigate gender differences. This two-step approach—beginning with an unbiased analysis and followed by a focused, candidate-based examination—was implemented given the limited sample size within each gender group.

Results

Demographic Features

Subjects with both MRI and SOFAS data were used in this study. In total, we analyzed the data from 118 study participants.

Table 1 shows the demographic summary of the study subjects. Overall, both high and low-functioning groups had more females than males, with a median age of 30. Additionally, males were split more evenly between the two groups while most females were in the high-functioning group.

Table 1 Demographics

	High SOFAS Score	Low SOFAS Score	Total
N	73	45	118
Sex			
Male	20	17	37
Female	53	28	81
Age			
Median	30	30	30
Range	18, 71	21, 64	18, 71
SOFAS Score			
Median	90	80	85
Range	82, 99	63, 80	63, 99

Brain structural differences between subjects with high and low social functioning

First, the volumes of subcortical regions were compared between the high and low-functioning groups. ANCOVA adjusting for age and sex yielded significant p-values for the right and left palladium (.0620 and .0549) (Table 2). The Benjamini-Hochberg process furthermore concluded significant adjusted p-values (0.035 for both), indicating significant deviation in pallidum volume between the high and low-functioning groups (Figure 1). Next, ANCOVA was conducted adjusting for age and sex and the Benjamini-Hochberg process to compare the surface area of cortical regions. The analysis found no significant differences across all regions between the high and low-functioning groups. Finally, the same process was conducted with the thickness of cortical regions. This yielded a significant p-value (0.0407) in the right frontal pole; however, the Benjamini-Hochberg process showed the result may be false positive with an insignificant adjusted p-value (0.963). Together, this study showed that the pallidum may be one region involved in social and occupational functions.

Table 2 Volume P Values

Brain Region	P Value	P Adjusted
Left Pallidum	0.003	0.049
Right Pallidum	0.007	0.052
Left Caudate	0.052	0.241
Right Caudate	0.080	0.272
Right Accumbens	0.098	0.273
Left Putamen	0.242	0.446
Right Putamen	0.255	0.446
Left Amygdala	0.283	0.446
Right Amygdala	0.287	0.446
Left Hippocampus	0.560	0.784
Right Hippocampus	0.750	0.920
Left Lateral Ventricle	0.826	0.920
Right Lateral Ventricle	0.855	0.920
Left Accumbens	0.977	0.977

Gender difference

Furthermore, the gender differences in the associations between social and occupational functions and pallidum were investigated. The analysis found significant p-values for the right (0.00788) and left pallidum (0.0129) in females. Males, on the other hand, were found to have no significant differences in the volume of pallidum between the high and low-functioning groups. Notably, the effect sizes of the changes in females were larger than the effect sizes of males, with Cohen's d values of 0.564 left and 0.604 right in females and 0.462 left and 0.464 right in males.

Discussion

Through an unbiased data-driven analysis, the pallidum was identified as a region with significant volumetric differences between individuals with high and low social and occupational

© The National High School Journal of Science 2024

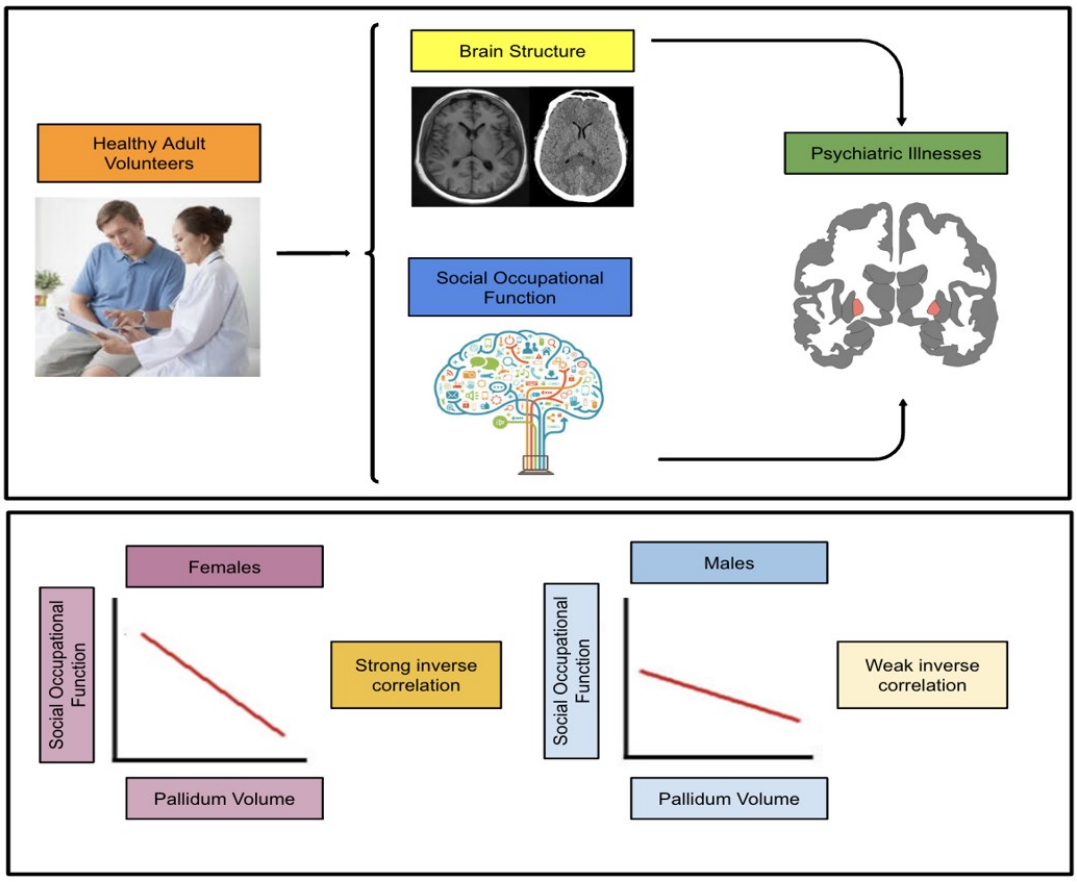

Fig. 1 Study design and main results: Healthy volunteers issued MRI scan and SID5-SOFAS examination. These factors have both individually been shown to correlate with psychiatric disorders. Results indicate females exhibit a strong correlation between SOFAS and pallidum volume whereas males exhibit a weak correlation.

functioning. Further targeted analysis focusing on pallidum identified a larger effect size of the associations between social and occupational functions and pallidum in females than in males.

The pallidum is a paired structure located within the basal ganglia and is known to be responsible for movement and functions as a reward mechanism. Moreover, studies found that pallidum may serve as an important 'limbic final common pathway' for mesocorticolimbic processing of reward and motivation[13]. The pallidum's involvement in reward systems may reveal its role in social and occupational function, as social cognition has been found to be associated with the reward system and reward pathways are activated when people are acknowledged for occupational[17] and intellectual contributions[18]. Furthermore, previous studies have found structural changes in the pallidum to be related to the diagnoses of neuropsychiatric diseases. For example, pallidum volumes were found to be greater in schizophrenia patients[19]. Additionally, it has been speculated that morphological alterations in the ventral pallidum are associated with social bonding disorders, such as autism, as it interferes with the limbic pathway[20].

Studies have shown that females display greater social and emotional awareness and function when compared to men[21]. Consistent with this study's findings, other research groups have also reported gender differences in the pallidum, discovering a larger pallidum volume in females[22]. It is important to note that the sample size of males in the NIMH dataset used in this research was smaller than that of females, which may have contributed to the insignificant results in males. Nevertheless, a larger effect size was observed in females, suggesting the potential sex differences in the involvement of pallidum in social and occupational functioning.

One strength of this study is the utilization of the OpenNeuro dataset to address key neuroimaging mechanisms underlying clinical phenotypes. Public datasets such as those from OpenNeuro foster greater scientific collaboration within the research community and enhance research study design, analysis, and operation[23]. This study may serve as a framework for how to utilize these open-source datasets to test key hypotheses. Furthermore, public data is not only a useful resource for researchers,

but also valuable to train students, facilitate learning, and allow them to explore and test their ideas about the world.

This study also includes several limitations, for example, all the subjects are healthy participants. Consequently, this study may not cover patients or individuals with extreme or severe social and occupational dysfunction. Future datasets with greater variability and larger sample sizes would help remedy this shortcoming. Another limitation is that this is a cross-sectional study. Longitudinal data with multiple time points[24] may provide more insights into the potential causal role of brain structural aberrations in social and occupational dysfunctions. Third, this study used data from 118 participants, with a gender imbalance—37 males and 81 females—which constrained the statistical power for gender-specific analyses. Larger, more balanced cohorts are needed to validate and expand upon observations from this study. Additionally, while this study highlighted the pallidum as a region of interest, the potential contributions of other brain regions to social and occupational function cannot be ruled out. Finally, the study cohort lacked information on socioeconomic status and education level, which are important factors that may influence social and occupational function. Future studies should collect more comprehensive data on participants' educational and socioeconomic backgrounds to address this gap.

Conclusion

The pallidum was identified to contain significant differences in volume between low and high social and occupational functioning groups. A gender difference was also found with significant changes in pallidum between high and low-functioning groups for females but no significance for males. This study shows the importance of the pallidum to future clinical implications in combatting psychiatric illnesses. Posteroventral pallidotomy (PVP), a treatment targeting the pallidum, has proven to be effective in reducing symptoms of Parkinson's disease[25]. Findings from this study suggest the great potential of these pallidum-targeted therapeutics for treating social and occupational dysfunction.

Methods

Study Participants

All participants in the NIMH dataset completed electronic consent forms before a pre-screening test. Additional written consent forms were provided for all other procedures. Only healthy adults were considered eligible to participate. To be considered eligible, all participants of the NIMH dataset were above the age of 18 and capable of speaking and understanding English. Requirements also stipulated participants have an IQ of 70 and above, passed 8th-grade education, did not possess a mental/suicidal history, and did not illicitly use drugs. Current employees of NIMH and their relatives were excluded from participation. Participants were recruited into the study through direct mailings, bulletin boards and listservs, outreach exhibits, print advertisements, and electronic media. These potential volunteers received a Structured Clinical Interview for DSM-5 Disorders (SCID-5), the Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), the Kaufman Brief Intelligence Test, Second Edition (KBIT-2), and the NIH Toolbox Cognition Battery through an in-person screening to check for particular mental or physical conditions.

Social Occupational Functioning Assessment Scale (SOFAS)

Eligible participants received a Structured Clinical Interview for DSM-5(SCID-5), which includes SOFAS. Used to gauge the level of social and occupational function of a patient, SOFAS derives its results from proficiency in the performance of daily tasks and interaction with society. Conducted in conjunction with the SCID-5, the scale more accurately compares results between healthy and unhealthy patients, since it does not account for the severity of psychological illnesses. Many studies have used this scale previously for studies, for example, to determine a relation between social and occupational function and depressive and psychotic symptoms[26]. DSM-5 has classified a SOFAS score of 90 to indicate good functioning, 80 to indicate slight impairment, and 70 to indicate difficulty in social, occupational, or school functioning[27]. Due to this study's cohort of only healthy subjects, the cutoff of 80 was selected between high(SOFAS ¿ 80) and low(SOFAS ¡ 80) functioning groups.

MRI Data

MRI is one frequently used non-invasive approach to detect brain structural changes. Many studies have utilized MRI data to investigate the underlying mechanisms of physiological processes and pathological conditions. MRI research has revealed abnormal brain structures associated with psychological illness and impaired brain function. For example, enlarged ventricular and pallidum have been observed in patients with schizophrenia. Structural changes in the anterior cingulate, subgenual prefrontal cortex, and amygdala have been observed in patients with bipolar disorder[28].

In the NIMH dataset, the MRI protocol involved a modified ADNI-3 basic protocol and included portions of the ABCD protocol. Specifically, the ADNI3 T1 scan was replaced with the ABCD T1 scan, fat saturation was turned on for the Axial T2 2D FLAIR acquisition from ADNI2 and the pCASL acquisition, high-resolution in-plane hippocampal 2D T2 scan was replaced with the whole brain 3D T2 scan from the ABCD protocol, the slice-select gradient reversal method was turned on for DTI acquisition, and reconstruction interpolation turned off, and scans for distortion correction were added. Participation in the MRI scan was optional for volunteers and required additional

© The National High School Journal of Science 2024

written consent.

FreeSurfer

We utilized FreeSurfer to process T1-weighted structural brain scans, following ENIGMA protocol (ENIGMA Subcortical Segmentation Protocols for Disease Working Groups: https://enigma.ini.usc.edu/protocols/imaging-protocols/). Automatic subcortical segmentation based on the Aseg atlas was performed. The volumes of subcortical brain regions as well as the surface area and thickness of cortical regions, were used in downstream statical analysis.

Statistical Analysis

R version 4.3.3 (2024-02-29) was used to conduct statistical analysis. We compared the brain measures between patients with high versus low social occupational functioning. Specifically, analysis of Covariance (ANCOVA) with age and sex as covariates was employed in this analysis. The Benjamini-Hochberg (BH) procedure was used for multiple comparison correction. Brain measures with adjusted p-values smaller than 0.05 were considered significant.

Acknowledgements

I would like to thank Professor Kun Yang from the Johns Hopkins University School of Medicine for her guidance and mentorship on the research for this paper.

References

1 O. Ybarra, P. Winkielman, I. Yeh, E. Burnstein and L. Kavanagh, *Friends (and Sometimes Enemies) With Cognitive Benefits: What Types of Social Interactions Boost Executive Functioning? Soc.*

2 B. Combs and K. Heaton, *Occupational Functionality: A Concept Analysis*.

3 E. D. Flood and F. in, 10.1007/978-3-319-31816-5_3059-1.

4 S. Kumari, S. Dahuja and U. Singh, *Association of clinical factors with socio-occupational functioning among individuals with schizophrenia*.

5 J. Koene, S. Zyto, J. Stel, N. Lang, M. Ammeraal, R. Kupka and J. Weeghel, *The relations between executive functions and occupational functioning in individuals with bipolar disorder: a scoping review*.

6 A. Brozgold, J. Borod, C. Martin, L. Pick, M. Alpert and J. Welkowitz, *Social Functioning and Facial Emotional Expression in Neurological and Psychiatric Disorders*.

7 A. Carswell and R. Eastwood, *Activities of Daily Living, Cognitive Impairment and Social Function in Community Residents with Alzheimer Disease*.

8 C. Feng, S. Eickhoff, T. Li, L. Wang, B. Becker, J. Camilleri, S. Hétu and Y. Luo, *Common brain networks underlying human social interactions: Evidence from large-scale neuroimaging meta-analysis*.

9 P. Metzak, M. Farris, T. Placsko, A. Braun, D. Bonneville, K. Brummitt, M. Chu and J. Addington, *Social functioning and brain imaging in individuals at clinical high-risk for psychosis: A systematic review*.

10 H. Wu, H. Yan, Y. Yang, M. Xu, Y. Shi, W. Zeng, J. Li, J. Zhang, C. Chang and N. Wang, *Occupational Neuroplasticity in the Human Brain: A Critical Review and Meta-Analysis of Neuroimaging Studies*.

11 Z. Narita, K. Yang, H. Kuga, P. Piancharoen, S. Etyemez, A. Faria, M. Mihaljevic, L. Longo, H. Namkung, J. Coughlin, G. Nestadt, F. Nucifora, T. Sedlak, R. Schaub, J. Crawford, D. Schretlen, J. Miyata, K. Ishizuka and A. Sawa, *Face processing of social cognition in patients with first episode psychosis: Its deficits and association with the right subcallosal anterior cingulate cortex*.

12 R. Adolphs, *What does the amygdala contribute to social cognition?*

13 K. Smith, A. Tindell, J. Aldridge and K. Berridge, *Ventral pallidum roles in reward and motivation*.

14 C. Markiewicz, K. Gorgolewski, F. Feingold, R. Blair, Y. Halchenko, E. Miller, N. Hardcastle, J. Wexler, O. Esteban, M. Goncavles, A. Jwa and R. Poldrack, *The OpenNeuro resource for sharing of neuroscience data*.

15 A. Nugent, A. Thomas, M. Mahoney, A. Gibbons, J. Smith, A. Charles, J. Shaw, J. Stout, A. Namyst, A. Basavaraj, E. Earl, T. Riddle, J. Snow, S. Japee, A. Pavletic, S. Sinclair, V. Roopchansingh, P. Bandettini and J. Chung, *The NIMH intramural healthy volunteer dataset: A comprehensive MEG, MRI, and behavioral resource*.

16 E. Healy, A. Reichenberg, K. Nam, M. Allin, M. Walshe, L. Rifkin, S. Murray and C. Nosarti, *Preterm Birth and Adolescent Social Functioning–Alterations in Emotion-Processing Brain Areas*.

17 S. Gutman and V. Schindler, *The neurological basis of occupation*.

18 T. Martinez, *Utilizing Worker Expertise and Maximizing The Brain Reward Centers*.

19 *Schizophrenia – what does structural MRI show? — Tidsskrift for Den norske legeforening*, https://tidsskriftet.no/en/2013/04/schizophrenia-what-does-structural-mri-show.

20 T. Napier and A. Mickiewicz, *The role of the ventral pallidum in psychiatric disorders*.

21 N. Romer, N. Ravitch, K. Tom, K. Merrell and K. Wesley, *Gender differences in positive social–emotional functioning*.

22 S. Inano, H. Takao, N. Hayashi, N. Yoshioka, H. Mori, A. Kunimatsu, O. Abe and K. Ohtomo, *Effects of age and gender on neuroanatomical volumes*.

23 P. Huston, V. Edge and E. Bernier, *Reaping the benefits of Open Data in public health*.

24 E. Caruana, M. Roman, J. Hernández-Sánchez and P. Solli, *Longitudinal studies*.

25 M. Merello, S. Starkstein, M. Nouzeilles, G. Kuzis and R. Leiguarda, *Bilateral pallidotomy for treatment of Parkinson's disease induced corticobulbar syndrome and psychic akinesia avoidable by globus pallidus lesion combined with contralateral stimulation*.

26 E. Monego, C. Cremonese, F. Gentili, P. Fusar-Poli, J. Shah and M. Solmi, *Clinical high at-risk mental state in young subjects accessing a mental disorder prevention service in Italy*.

27 D. S. M. M. D. Fourth, *Text Revis, American Psychiatric Association (2000)*.

28 E. Serap Monkul, G. Malhi and J. Soares, *Anatomical MRI Abnormalities in Bipolar Disorder: Do They Exist and Do They Progress?*