The impact of executive functioning deficit on illness severity in patients with an ADHD diagnosis: a real-world data study

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BACKGROUND

- Executive functioning (EF) is a multifaceted neuropsychological construct that subserves goal-directed and novel problem-solving behaviors.[1]
- Deficits in EF are commonly identified in individuals with ADHD[2,3], however, moderate effect sizes and the lack of universality in EF deficits in previous meta-analyses[4, 5] suggest that deficits in EF are only be present in a subgroup of individuals with ADHD.
- Interpretations of meta-analyses are often complicated due to the differences in sampling procedures, operationalization of variables, and covariates, resulting in multivariate effects estimated from a heterogenous sample[6].
- The use of large real-world datasets generated from Electronic Health Records (EHR) may provide unique insights on the prevalence and impact of EF deficits in ADHD.
- **Objective**: This study aimed to examine EF deficits and their association to general illness severity (measured by the Clinical Global Index- Severity (CGI-S) scale in a cohort of patients with ADHD, based on clinical documentation in real-world settings.

RESULTS

- Of the total cohort (n=17,420) with an ADHD diagnosis, 3.3% had clinically documented deficits in EF.
- The average age of diagnosis was younger for the group with documented EF deficits (M=16.9yrs, SD=12.6) versus those without EF deficits (M=17.8yrs, SD=13.0, $p = .018$).
- Higher CGI-S scores at baseline were observed for ADHD with EF deficits (M=4.7, SD=1.0) versus those without EF deficits (M=4.4, SD=1.0, $p < .0001$).
- Results of a multivariate regression analysis are shown in Table 1. Demographic features that were associated with an increased risk of EF deficits included: Male gender, Hispanic or Latino ethnicity, older age and increased CGI-S score.

Table 1. The association of demographic characteristics and the presence of executive functioning deficits in patients with a diagnosis of ADHD (n=17,420). Analysed using a multivariate logistic regression. Note age and CGI-S were treated as continuous variables

Variables		N(%)	OR	95% CI	*p*- value
Gender	Reference: Female	6967 (40.0)			
	Male	10453 (60.0)	1.44	1.20 to 1.73	< 0.001
Race	Reference: White	13643 (78.3)			
	American Indian or Alaska Native	65 (0.4)	0.94	0.23 to 3.86	0.930
	Asian	56 (0.3)	1.73	0.53 to 5.57	0.361
	Black or African American	2609 (15.0)	1.22	0.97 to 1.54	0.082
	Native Hawaiian or Other Pacific Islander	241 (1.4)	0.22	0.08 to 0.62	0.004
	Other Race	806 (4.6)	0.21	0.11 to 0.42	< 0.001
Ethnicity	Reference: Not Hispanic or Latino	15973 (91.7)			
	Hispanic or Latino	1447 (8.3)	2.55	1.95 to 3.34	< 0.001
		Mean (SD)			
Age	(years)	18.33 (13.36)	1.01	1.00 to 1.01	0.032
CGI-S	Integer score (1-7)	4.38 (1.03)	1.50	1.37 to 1.64	< 0.001

Proportion of ADHD with executive functioning deficits

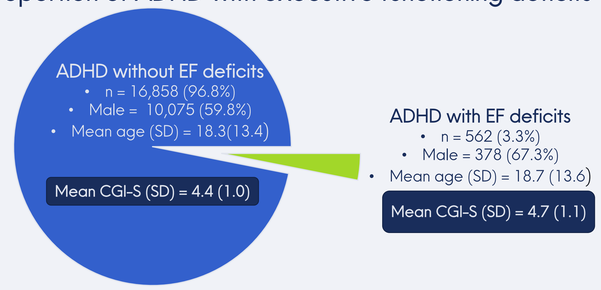

Figure 1. Baseline demographic characteristic and illness severity of patients with a diagnosis ADHD stratified by those with and without EF deficits. Illness severity was analyzed using the Clinical Global Index - Severity (CGI-S) scale (n=17,420).

METHOD

Data source:

NeuroBlu™ database

50+ million rows of patient data | **560K+** Patients | **20+ years** Longitudinal Data

Structured Data

- Outcome Measures (e.g., CGI-S, GAF)
- Diagnosis Codes (ICD-9, ICD-10)
- Prescription Data
- Patient Demographics
- Emergency Department, inpatient & outpatient data across the same patients in 20 of 25 clinics

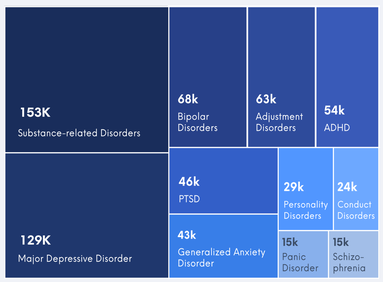

Figure 1. NeuroBlu Database overview

Unstructured Data

Mental Status Examination (MSE)

- Categorized notes on patient's function, appearance and mood at a visit
- Holmusk developed >30 advanced Neural Network models to predict structured labels from MSE
- Created >300 psychiatry specific labels in collaboration with clinicians to track disease progression over time

External Stressors

Social, relational and occupational events that may affect the patient's mental health

Inclusion Criteria:

- Diagnosis of ADHD (ICD-9: 314.00, 314.01; ICD-10: F90.*)
- At least one record of CGI-S +/- 14 days of initial ADHD diagnosis (index date)
- Patients with unknown race or gender were excluded

Cohort definition:

Clinical information in the free text of the Mental State Examination (MSE) was captured using Natural Language Processing (NLP) techniques and used to define two groups: **ADHD with deficits in EF and ADHD without deficits in EF**

Analysis:

- Welch's two-sided t-test: Between-group comparison in baseline CGI-S scores between ADHD with EF deficits versus those without
- Multiple logistic regression was used to identify demographic and clinical features associated with EF deficits

Data Source of US Health Facilities

De-identified EHR data were obtained from U.S. mental health services that use the MindLinc EHR system. The data were analysed in NeuroBlu, a secure Trusted Research Environment (TRE) that enables data assembly and analysis using an R/Python code engine.

The NeuroBlu platform has received a waiver of authorisation for analysis of deidentified healthcare data from the WCG Institutional Review Board (Ref: WCG-IRB 1-1470336-1).

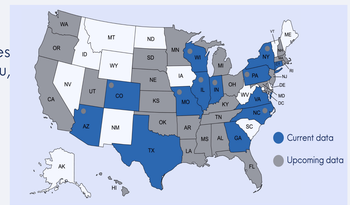

Figure 2. State specific data source for NeuroBlu

DISCUSSION

- Our results suggest that EF deficits are clinically documented in only a small proportion of patients with ADHD. Our results support findings that not all individuals with ADHD present with deficits in EF.[7] However, they are at odds with findings using EF rating scales that report much higher proportions of EF deficits[7,8].
- This discrepancy suggests that EF deficits may not be apparent without applying a specific measure, EF rating scales should therefore be used when assessing adults with ADHD to gain a full understanding of how the disorder may impact daily life.
- While earlier theories have proposed deficient inhibitory control as a core deficit in ADHD which secondarily disrupts other EF processes[8], more recent reviews have found only modest associations between a range of EF deficits and ADHD[4].
- Studies have also shown that little evidence for EF deficits in ADHD remain after controlling for non-executive abilities[9, 10].
- EF deficits were more prevalent in those with a higher degree of illness severity for individuals with ADHD.
- One limitation of this study is that specific domains of EF were not examined in the cohort as these are not routinely recorded within the dataset.
- Certain types of EF deficits have been replicated more consistently across ADHD samples, e.g., deficits in executive motor inhibition and working memory manipulation[11, 12].

Conflict of Interest: All authors report current employment with Holmusk Technologies, Inc. SHK, MV, and RP report equity ownership in Holmusk Technologies, Inc

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