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ORIGINAL ARTICLE

ATTENTION DEFICIT HYPERACTIVITY DISORDER, BIPOLAR DISORDER, DIABETES MELLITUS, AND PARKINSON'S DISEASE: COMMON FACTORS

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Abstract

Importance

A disclosure of pathogenic factors common to attention deficit hyperactivity disorder (AD), bipolar disorder (BP), diabetes mellitus (DM), and Parkinson's disease (PD).

Objective

The purpose of this survey is to compare inheritance patterns of AD, BD, DM, and PD and their associations with Dupuytren's contracture (DC), trigger finger (TF), and fingernail dystrophy (ND).

Interventions

Elderly residents of a retirement community - selected for AD, BD, DM, or PD - were questioned for a history of these disorders in their families - in the preceding, current, and following generations. These residents were also examined for DC, TF, and ND.

Results

Thirty-three residents, aged 50 to 91, median 84 years, representing 441 family members (208 male, 233 female) were examined.The disorders of these residents were9 AD, 2 BD, 5 DM, 17 PD.

Hand examinations were positive for 1 or more signs in 22of 32subjects so examined (69%) with 14 DC, 10 TF, and 8 ND. The disorders found among all family members, were 34 AD, 25 BP, 22 DM, and 24 PD for a total of 105, or 24% of all family members. The distribution of these disorders was mixed in 27 families, unmixed or single in 6.

Conclusion

AD, BP, DM, and PD occur together in families, seldom as unmixed -

suggesting common genetic factors. Elderly subjects with any of these disorders often have DC, TF, or ND - suggesting common pathophysiology.

Introduction

Various papers have shown a familial coincidence between attention deficit hyperactivity disorder (AD) and diabetes mellitus (DM), between bipolar disorder (BP) and DM, and between Parkinson's disease (PD) and DM [1-4]. These associations with DM, while modest at about 20 percent, suggest that AD, BP, DM, and PA may be related to each other, that some pathophysiologies may be held in common. In the following survey of retirement home residents it will be shown that inheritance of these neuroendocrine disorders over 3 generations is more often mixed than unmixed or "pure," implying shared genetic factors.

The hand signs Dupuytren's contracture (DC), trigger finger (TF), and fingernail dystrophy (ND) are often, though not exclusively, associated with DM [5-7], one of the disorders of interest. This survey of retirement home residents will show these hand signs similarly prevalent with AD, BP, DM, and PD.

In summary, a survey of elderly individuals with AD, BP, DM, or PD will suggest common pathophysiologies as evidenced by shared inheritance patterns and prevalent and signs.

Methods

Subjects

Probands were residents of a retirement community diagnosed with AD, BP, DM, or PD after informed, written consent. *These residents were questioned for a lifetime history of AD, BP, DM, and PD in themselves and their families. These residents were also examined for DC, TF, and ND. There was no attempt to measure the prevalence of these disorders or of hand signs in this retirement community. The purpose was to 1) test the overlap in the inheritance of AD, BP, DM, and PD over 3 generations and 2) to determine the prevalence of DC, TF, and ND associated with these disorders in the probands.

The probands were questioned in a standardized manner for the presence or absence of the proposed cluster of disorders in themselves and their families. A family consisted of each member of the previous, current, and following generation - the proband's parents, uncles, and aunts, siblings, and children. Cousins, nieces, and nephews were not included. A family member was excluded from the survey if the index subject believed his or her memory of the relative was insufficient or if the relative had died in childhood. The following criteria for a diagnosis applied to both the subjects interviewed and to the associated family members.

AD was diagnosed if short-term memory deficit, exceptionally high physical activity or impulsive, sometimes inappropriate behavior was observed in the proband or recalled by the proband in his/her childhood or in a relative. The diagnosis was applied to children or to adults, persisting since childhood.

* Two probands were residents of other communities.

The diagnosis of BD was accepted if the term "depression" was used by the proband and treatment had been required, or employment had been affected, or a Suicide attempt, successful or unsuccessful, had been reported. Mania by name was not asked about. However, uncontrolled behavior such as obsessive gambling was classified with BD, if instances of depression had been reported in addition. In the individual with a recurrence of BD the number of disorders was counted as 1.

The presence of DM was accepted by name alone if treatment with medication or by weight loss had been prescribed. No attempt was made to distinguish Type I from Type II diabetes. When "hypoglycemia" had been diagnosed as such and treatment required, this condition was classified as pre-diabetic and grouped with DM as has been previously reported [8].

The presence of PD was accepted in the proband if PD had previously been diagnosed and if treatment had been required or if tremor at rest had developed in the later adult years, or reduced motion of the upper extremities had been observed.

An examination of the hands of the probands was carried out. Dupuytren's contracture (DC) was diagnosed by the scarring at or near the base of the fourth finger. Trigger finger (TF) was diagnosed by the description of a "catching" of the fingers on opening the hand from a grasping position or by demonstration of the catching on examination. Fingernail dystrophy (ND) was diagnosed by the presence of deformed, broken nails and a history of longstanding breakage of the nails or of chewing the nails as an adult.

Assessment

A Pearson correlation analysis was conducted to determine whether a disorder of one kind in a family is more likely to be associated with a disorder of another kind than with a disorder of the same kind within a given family. Proband's with hand signs were counted and described.

Results

Thirty-three probands and their families were assessed, Table1.

It can be shown that within family, neuroendocrine disorders usually differed, were seldom the same.

The Pearson correlation analysis to determine whether a disorder of one kind was more likely to be associated with a disorder of a different kind within a family showed a significant correlation between the different disorders, $p < 0.05$ (Table 2).

Hand signs could be demonstrated with equal frequency in proband's with AD, BP, DM, and PD (Table 3).

An incidental result of this survey is displayed, Table 4 and 5. Five individuals had sustained more than 1 of neuroendocrine disorder in their lifetimes. The earliest disorder was AD or BP and the latest DM or PD. The order of occurrence of these disorders was consistent in each individual.

Discussion

The prevalence of AD, BP, DM, and PD in a general population or even in the retirement community surveyed cannot be inferred from the data presented.

The selection of individuals for interview depended upon casual observation by the investigator, who sought index cases of AD, BD, DM, and PD. Evidence has been presented that AD, BP, DM, and PD occurs frequently, 24% of family members, but randomly. The failure to find unique inheritance patterns for AD, BP, DM, or PD can be reconciled by suggesting that these disorders emanate from common genetic factors [1-4] programming shared pathophysiologies.

An example of common pathophysiology that can be cited

Table 1: Characteristics of families surveyed

Probands (Families)	33
Age of probands	50 - 91, 84
Families/generations	33/97*
Male/Female subjects	208/233
Subjects, total	441
Attention deficit hyperactivity disorder	34
Bipolar disorder	22
Diabetes mellitus	25
Parkinson's disease	24
Disorders, total	105 (23.8%)

*Two probands had no children, no succeeding generations

Table 2: Families with mixed vs. unmixed neuroendocrine disorders

	Attention Deficit	Bipolar Disorder	Diabetes Mellitus	Parkinson's Disease	Total
Families (n)	9	2	5	17	33
Mixed disorders	34	19	24	18	95
Unmixed disorders	0	3	1	6	10
Total disorders	34	22	25	24	105

Table 3: Results of Pearson Correlation Analysis of Association between Variables

	DM	BP	AD	Total disorders	Negative disorders	Total Family Members
PD Pearson Correlation	0.43	0.24	-0.77	0.27	0	0.07
Sig. (2 tailed)	0.05	0.31	0.77	0.24	0.99	0.78
N	21	21	21	21	21	21
DM Pearson Correlation		0.39	0.14	0.52*	-0.27	-0.11
Sig. (2 tailed)		0.08	0.55	0.02	0.24	0.64
N		21	21	21	21	21
BP Pearson Correlation			0.41	0.90*	-0.22	-0.03
Sig. (2 tailed)			0.07	0	0.34	0.88
N			21	21	21	21
AD Pearson Correlation				0.62*	-0.05	0.14
Sig. (2 tailed)				0	0.84	0.55
N				21	21	21
Total Pearson Correlation disorder					-0.24	0.1
Sig. (2-tailed)					0.29	0.95
N					21	21
Negative Pearson Correlation						0.93*
Sig. (2-tailed)						0
N						21

*Correlation is significant at the O.05 level (2-tailed). Within families each disorder is more likely to be associated with a different disorder than with the same disorder.

Table 4: Hand signs in neuroendocrine disorders

Disorder	Positive Exams/Subject	Hand signs		
		DC	TF	ND
AD	8/8*	7	4	2
BP	2/2*	2	1	1
DM	3/5*	32	3	
PD	9/17*	9	6	4
Totals	22/32	20	13	10

22 of 32 subjects examined (69%) had at least 1 hand sign.*The hands for 1 proband, not included, were not examined and were not counted for this comparison

Table 5: Disorders in individuals by relative time of occurrence.

Individual	Earliest to Last Disorder
1	AD, BP, DM, PD
2	BP, DM
3	AD, PD
4	AD, DM
5	AD,DM

is insufficient control of circulation. Hypotension has been commonly noted in children with AD [9]. Fluctuations in cerebral blood flow to either side have been associated with BD [10, 11]. Variations in vascular tone are common with treated diabetics, related to depleted epinephrine stores [12]. Extreme variations in cerebral blood flow un attributable to orthostatic hypotension are noted in PD [13].

Still further similarities among these disorders are related to catecholamine metabolism. Adreno medullary function is important in AD and is correlated with the mood swings of BD [14, 15]. In addition, it can be pointed out that both DM and PD are associated with atrophy of the adrenal medulla, the major source of epinephrine as a hormone [16, 17].

More direct similarities noted among AD, BP, DM, and PD have been described by the abnormalities of the hand - DC, TF, ND -noted in this survey. Although DC, TF, ND is usually described for diabetes mellitus, they have been noted in this survey in subjects with the neuroendocrine disorders AD, BP, DM, and PD. Given that these hand signs are associated with microvasculopathy on histological examination of the afflicted hands, an implication is that AD, BP, DM, and PD share this pathology [18- 20]. In fact, examination of other tissues, notably the brain, has revealed microvasculopathy in BP, DM, PD [21-23]. An exception may be AD. It is possible that as this disorder is recognized to extend for a lifetime a similar cerebral pathology will be reported.

The consistent order of the onset of AS, BP, DM, and PD in individuals noted incidentally is roughly consistent with the onset of these disorders in general populations. This incidental observation supports a concept of accumulating effects of a pathophysiology beginning with AD and progressing to PD.

Some limitations to this study can be pointed out. The validity of diagnoses can be questioned because of the brevity of diagnostic criteria and the lack of personal interview and direct examination of family members. It is believed, however, that a proband's recall of unusual physical activity or depression, terms which are familiar to most laypersons, is accurate, and the requirement for a significant consequences of these disorders - such as learning disability, medication, work failure, or suicide attempt - are validating. Diabetes is almost always accurate since the diagnosis is objective with laboratory testing. PD in the early stages may be controversial but most subjects with this diagnosis were previously diagnosed and under treatment.

The evidence for familial clustering of some neuroendocrine disorders, their progressive nature, and the evidence for microangiopathy in older persons with these disorders should stimulate a more inclusive concept of their causes.

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References

1. Ji J, Chen T, Sundquist J, Sundquist K. Type 1 diabetes in parents and risk of attention deficit hyperactivity disorder in offspring: a population-based study in Sweden. Diabetes Care. 2018.
2. Russell JD, Johnson GE. Affective disorders, diabetes mellitus and lithium. Aust N Z J Psychiatry. 198l; 15: 349 - 353.
3. Chang JC, Yen AM, Lee CS, et al. Metabolic syndrome and the risk of suicide: a community-based integrated screening samples cohort study. Psychosom Med. 2013; 75: 807 - 814.
4. D'Amelio M, Ragonese P, Callari G, et al. Diabetes preceding Parkinson's disease onset. A case-control study. Parkinsonism

Relat Disord. 2009; 15: 660 - 664.

5. Chammas M, Bousquet P, Renard E, et al. Dupuytren's disease, carpal tunnel syndrome, trigger finger, and diabetes mellitus. J Hand Surg. 1995; 20: 109 - 114.

6. Zatz R, Brenner BM. Pathogenesis of diabetic microangiopathy. The hemodynamic view. Am J Med. 1986; 80: 443 - 453.

7. Pandey A, Usman K, Reddy H, et al. Prevalence of hand disorders in type 2 diabetes mellitus and its correlation with microvascular complications. Ann Med Health Sci Res. 2013; 3: 349 - 354.

8. Seltzer H, Fajans S,Conn J. Spontaneous hypoglycemia as an early manifestation of diabetes mellitus. Diabetes. 1956; 5: 437 - 439.

9. Tommaso MC. A comparative study of bipolar disorder and attention deficit hyperactivity disorder through the measurement of regional cerebral blood flow. J Biol Regul Homeost Agents. 2012; 26: 1 - 6.

10. Paranthaman R, Greenstein AS, Burns, et al. Vascular function in older adults with depressive disorder. Bio Psychiatry. 2010; 68: 133 - 139.

11. Direk N, Koudstall RJ, Hofman A, et al. Cerebral hemodynamics and incident depression: the Rotterdam study. Biol Psychiatry. 2012; 15: 318 - 323.

12. Tack CJ, Smits P, Willermsen JJ, et al. Effects of insulin on vascular tone and sympathetic nervous system in NIDDM. Diabetes. 1996; 45: 15 - 22.

13. Park J, Kim HT, Park KM, et al. Orthostatic dizziness in Parkinson's disease is attributed to cerebral hypoperfusion: a transcranial doppler study. 2017; 45: 337 - 342.

14. Anderson GM, Dover MA, Yang BP, et al. Adrenomedullary function during cognitive testing attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2000; 39: 635 - 643.

15. Maas JW, Katz MM, Koslow SH, et al. Adrenomedullary function in depressed patients. J Psychiat Res. 1994; 28: 357 - 367.

16. Brown FM, Zuckerman M, Lonway S, et al. Adrenal medullary fibrosis in IDDM of long duration.Diabetes Care. 1989; 12: 494 -4 97.

17. Stoddard SL.The adrenal medulla and Parkinson's disease. Rev Neurosci. 1994; 5: 293 - 307.

18. Kischer CW, Speer DP. Microvascular changes in Dupuytren's contracture. J Hand Surg Am. 1984; 9A: 58 - 62.

19. Uchihashi K, Tsuruta T, Mine H, et al. Histopathology of tenosynovium in trigger fingers. 2014; 64: 276 - 282.

20. Pazos-Moura CC, Moura EG, Bouskela E, et al. Nailfold capillaroscopy in diabetes mellitus: morphological abnormalities and relationship with microangiopathy. 1987; 20: 777 - 780.

21. Direk N, Koudstaal P, Hofman A, et al. Cerebral hemodynamics and incident depression: the Rotterdam study. 2012; 72: 318 - 323.

22. Li Y, Zeng KW, Wang XM Cerebral microangiopathy of diabetes. 2017; 42: 2247 - 2253.

23. Hatate J, Miwa K, Matsumoto M, et al. Association between cerebral small vessel diseases and mild parkinsonian signs in the elderly with vascular risk factors.

24. Parkinsonism Relat Discord. 2016; 26: 29 - 34.