Impact of Medical Academic Genealogy on Publication Patterns: An Analysis of the Literature for Surgical Resection in Brain Tumor Patients

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Background:

"Academic genealogy" refers to the linking of scientists and scholars based on their dissertation supervisors. We propose that this concept can be applied to medical training and that this "medical academic genealogy" may influence results reported in publications.

Methods:

We performed a comprehensive PubMed search to identify U.S. authors who have contributed peer-reviewed articles on a neurosurgery topic that remains controversial: the value of maximal resection for high grade gliomas (HGGs). Training information for each key author (defined as the first or last author of an article) was collected (including the author's medical school, residency, and fellowship training). Authors were recursively linked to faculty mentors to form genealogies. Correlations between genealogy and publication results were examined.

Results:

Our search identified 108 articles with 160 unique key authors. Authors who were members of two genealogies contributed to 38% of all articles studied. If an article was written by one of the 14 authors from the first genealogy, its results were more likely to support maximal resection even when we corrected for confounders (LOR 2.20, $p<0.044$). In contrast, if an article was written by one of the 8 authors from the second genealogy, it was less likely to support maximal resection (LOR -1.54, $p<0.024$).

Conclusions:

Authors related by medical academic genealogy made significant contributions to the literature on surgical resection for HGGs. Genealogies were identified where membership associated with reported results. These findings have important implications for the interpretation of scientific literature, design of medical training, and health care policy.

Keywords: medical academic genealogy, medical education, extent of resection, high grade glioma, brain cancer, network analysis

INTRODUCTION

A central tenet of science is that investigators should strive to be objective – to be free from the undue influence of past experience, social context, and the opinions of peers and mentors. Basic intuition, however, suggests that perceptions and conclusions are likely affected by the beliefs of those around us, particularly our mentors. This intuition is supported by a well-established literature in both the social sciences[1–6] and the physical sciences[5–10]. In particular, an emerging interdisciplinary literature suggests that mentors and mentoring environments have a strong influence on researcher attitudes, methods of investigation, and career development[11–14].

To date, studies investigating social factors that influence scientific and investigations tend to use qualitative methodologies. The notion of "academic genealogy", in which scientists are linked based on their dissertation supervisors, is one technique designed to qualitatively characterize the influence of mentors[15–19]. Genealogies have also been constructed to analyze other creative fields such as philosophy[20], music[21], and art[22,23] to follow the influences of teachers on their students. The emergence of dynamic network models[24,25] and social network analysis[26–28] now allow rigorous quantitation of genealogical influences. Here, we apply the concept of academic genealogy to medical training and use network analysis to quantitatively assess the impact of "medical academic genealogy" on medical investigations.

To this end, we study the medical academic genealogy of authors who contributed peer-reviewed articles on a controversial subject in neurosurgery, the utility of maximal surgical resection in patients afflicted with high grade gliomas (HGGs)[29–35]. The infiltrative nature of high grade gliomas, the most common forms of adult brain cancer, renders complete surgical resection impossible. The unresolved issue, however, is whether maximal resection leads to increased survival. Supporters of maximal resection believe that reducing the tumor burden

enhances the efficacy of subsequent chemo-radiation[32]. Opponents argue that this is of no benefit given the inherent resistance of HGGs to chemotherapy and radiation[33]. While the number of retrospective studies exploring this issue has greatly increased in recent years[34,35], the controversy has not been resolved through a well-designed randomized clinical trial.

The goal of this study is to use this controversy to examine whether medical training genealogy influences published results. Utilizing quantitative network analysis, we find a statistical association between membership in a genealogy and results published in this field.

METHODS

Identification of key articles. A comprehensive PubMed search was performed in December of 2014 using broad terms relating to this controversy (see **eTable1**). This process identified 4047 articles for review. Articles were then selected for this study if they were i) written in English, ii) published before December 2014, iii) presented original research results on human patients, iv) focused on adult intracranial HGGs, v) addressed the issue of maximal resection, vi) were written as a clinical study and not a case report, vii) used mortality as an outcome, viii) performed a univariate or multivariate statistical analysis and ix) considered maximal resection as a separate comparison group in their statistical analysis and x) listed a primary address at an American institution for either the first or last authors (see **eFig1**). The last criterion was necessary because it was often not possible to ascertain and verify the training history of authors trained at foreign institutions. This process produced 108 articles for analysis (see **eTable2**). We classified these articles into two groups. Those that found a statistically significant correlation ($p<0.05$) between maximal resection and survival as a primary or secondary result were labelled “supportive”. Those that reported no statistical association between maximal

surgical resection and overall survival were labelled "not supportive". All included articles were read by two independent readers (B.R.H. and J.A.T) and discrepant articles (**eTable3**) were discussed with senior readership (C.C.C).

Author classification. Following convention, we defined the first and last author of each article as "key authors", with the rationale that these authors play key roles in data analysis and manuscript preparation[36]. To avoid oversampling from the small number of articles with joint first or last authorship, we selected only the first and the last of the co-authors for our study. There were 160 unique key authors of our 108 articles because many authors were key authors of more than one article (see **eTable4**). Internet searches were performed to determine their medical subspecialty (if any) as well as the timing and location of their medical school, residency, and fellowship training. All information was compiled (by B.R.H. and J.A.T.) using publicly available academic or institutional resumes and verified against publicly accessible documents such as academic directory listings, alumni pages, and press briefings. Each training history was verified using at least two independent sources.

Construction of medical academic genealogies. We adopted a "top-down" approach to identifying medical academic genealogies. We first identified as potential "founders" the 21 authors who served as department chairmen because these individuals oversee the training of multiple trainees. Next, we linked these potential founders to their trainees, trainees of trainees, and so on in a recursive manner to create what social network analysis calls the "ego network" of the chairmen[24,26,27]. Links were drawn between authors if one was a faculty member at an institution while another was a trainee (medical student, resident, or fellow) in the same

discipline. To be connected, mentor and trainee had to be located at the same institution during the same calendar year, and the interaction had to occur after the founder became chairman. This process produced nine medical academic genealogies for analysis (see **eTable5** and **eTable6**).

Association of genealogy and articles. Many of the key authors were middle authors of manuscripts for where they did not serve first or last author (see **eTable7**). To capture the influence of these authorships, we considered an article to have been written by a member of a genealogy if an article had an author (including middle authorships) who was a member of that genealogy. In analyzing the articles produced by a genealogy, we only counted an article once no matter how many authors were members of that genealogy. On the other hand, if an article included members of multiple genealogies, it was included in the analysis of each (see **eTable8**). We applied similar criteria in classifying articles by medical subspecialty. For example, we considered an article to be written by a member of a specialty if it had one of our key authors from that specialty on the article, even if he or she was a middle author.

Univariate controls. Because prior qualitative literature has suggested that later publications are more likely to support maximal resection[34,35], we divided the articles into those published in this decade (2010 and later) and those published earlier. We chose this date because approximately half of the manuscripts were published before and after it. In addition, because the literature suggests that larger study populations are associated with a higher likelihood of support for maximal resection[34,35], we also corrected for publication sample size. Because of the right-skew nature of the data, it was necessary to perform a logarithmic conversion of the sample size before statistical modeling (see **eTable8**).

Analysis. We performed a series of Fisher exact tests to determine whether each genealogy produced a set of articles that differed statistically from the general literature in its support for maximal resection. Holm-Bonferroni correction was performed for multiple comparisons. For genealogies with univariate significance, logistic regression was used to correct for known literature controls. We also created a multivariate model using all significant univariate terms. Finally, we used the statistical machine learning technique LASSO (Least Absolute Shrinkage and Selection Operator)[37,38] to identify the suite of the variables most predictive of support for maximal resection (see **eTable9**). Statistical analysis was performed R version 3.1.2 (R Foundation for Statistical Computing) and p values less than 0.05 were considered significant. Visual representation of these genealogies were created using *ORA version 3.0.9 (CASOS center, Carnegie Mellon University).

RESULTS

Description of articles, authors, and founders, and genealogies. Our search identified 108 original articles, 160 key authors, and 9 genealogies that met our inclusion criteria (**Table 1**, **eTables 2-5**). A majority of the articles (70%) reported a statistically significant survival benefit of maximal resection for HGG patients. Articles published after 2010 and articles with larger study populations were more likely to support maximal resection.

Association between genealogy and publication result. A univariate analysis was performed for each of the nine potential genealogies to determine whether articles with one or more co-authors from the genealogy were statistically associated with results (first column, **Table 2**).

After Holm-Bonferonni correction for multiple comparisons[39], we found that two genealogies were associated with publication outcome (**Figure 1**). One genealogy was founded by Dr. Berger, the current neurosurgical chair at the University of California San Francisco. The presence of one or more authors from this genealogy increased the log odds of support for resection by 2.76 (corrected $p<0.004$). The second genealogy was founded by Dr. Phillips, the former radiation oncology chair at the University of California San Francisco. The presence of one or more authors from this genealogy decreased the log odds of support resection by -1.69 (corrected $p<0.035$).

Disproportionate impact of these genealogies on published literature. Members of the Berger and Phillips genealogies were responsible for a substantial portion of the literature studied (**Table 3**). Our analysis revealed that genealogy members represented only 14% of all key authors (9% Berger lineage and 5% Phillips lineage), but that authors from these lineages were co-authors on 38% of all articles studied (25% from Berger lineage, 13% from Phillips lineage).

Association persists after correction for covariates. Qualitative reviews have suggested that both more recent studies and studies with larger patient cohorts are more likely to support maximal resection[34,35]. Our univariate results support these suppositions (first column, **Table 2**). We find, however, that medical academic genealogy is an important predictive factor even after controlling for these covariates (second and third columns, **Table 2**). The presence of one or more Berger lineage authors increased the log odds of a supportive result (LOR 2.20, $p<0.044$) while the presence of one or more Phillips lineage authors decreased it (LOR -1.54, $p<0.024$).

Association is not due to medical specialty. To evaluate whether our genealogy findings were simply a reflection of medical specialty, we constructed additional models to evaluate whether the results of articles co-authored by members of a medical specialty differed from the remainder. Articles written by key author neurosurgeons (corrected $p>0.816$) or medical oncologists (corrected $p>0.999$) did not differ (first column, **Table 2**). While articles written by radiation oncologists were less likely to support maximal resection (LOR -1.14, corrected $p<0.039$), this finding was not significant after correction for known covariates ($p>0.103$, fourth column, **Table 2**).

Multivariate models. We performed two multivariate analyses. A multivariate model using all significant univariate predictors (publication date during/after 2010, sample size, presence of at least one key author radiation oncologist, and presence of an author from one of the two identified genealogies) found a trend for but no statistical significance of genealogy for both the Berger ($p>0.071$) and Phillips ($p>0.075$, fifth column, **Table 2**). We also performed a LASSO model starting with all univariate predictors, including those that did not have univariate significance (see **eTable9**). LASSO is a machine learning regression algorithm designed to identify key variables that associate with outcome in an unbiased manner. The LASSO model indicated that time of publication, article sample size, and the two previously identified genealogies were the best coefficients (last column, **Table 2**). Statistical analysis of the LASSO model found that article sample size (LOR 1.28, $p < 0.018$) and presence of an author from the Phillips lineage (LOR -1.35, $p<0.048$) were independently associated with article result.

DISCUSSION

Using a quantitative methodology derived from social network analysis, we demonstrate that publication outcomes on the question of the value of surgical resection for high grade glioma are statistically associated with that the training history of medical investigators (their "medical academic genealogy"). We therefore suggest that medical academic genealogy plays a previously unrecognized role in shaping the medical literature. While our study examines a specific neurosurgical topic, the issues we raise are pertinent to critical evaluation of all peer-reviewed literature. We recognize that any bias due to medical academic genealogy may be magnified in fields such as neurosurgery, where mentor-mentee relationships are hierarchical. However, we believe that such effects may be present in other fields. In this context, medical investigators should look for these genealogical effects when evaluating the literature just as we look for other types of bias[2,5], sequestration of evidence[7] and conflicts of interest[3].

Our findings have particular significance in the era of health reform. Increasingly, the effectiveness of medical practice will be evaluated by central panels who review the published literature. Care should be taken in the evaluation of medical literature disproportionately shaped by members of medical academic genealogies. Further, the potential influence of medical academic genealogy on publication outcome challenges a fundamental premise of meta-analyses, since each individual publication may not represent an independent investigative unit[40]. The development of statistical tools that adjust for the influence of genealogy may be needed for future quantitative reviews.

Our results also highlight an inherent tension in medical mentorship. While in clinical care it often necessary to have hierarchical interactions, in research we should strive to foster independence. The challenge of medical training lies in fostering appropriate mentor-mentee

relationships while minimizing the unconscious adaptation of mentor biases. It may therefore be necessary to consciously structure the educational experience to reflect these goals. In this context, an integrated educational approach involving thoughtful curriculum design, mentor self-awareness, and training individualized to the tendencies of the trainee will be necessary to minimize genealogical bias.

There are several limitations inherent in our study design. Like as in all retrospective studies, our conclusions were based on correlative associations with causation inferred. Furthermore, we recognize that dividing complex variables into discrete groups may have potential impact on statistical analysis. The genealogies which we study are abstractions of a complex medical community, and the exclusion of non-U.S. authors potentially limits the generalizability of our conclusion. In addition, although our analysis weights all educational links equally, though the literature suggests that mentor influence vary during training[11]. Despite all this, we believe that our data compellingly demonstrate the effects of medical academic genealogy on published peer-reviewed literature.

CONCLUSION

Analysis of the peer-reviewed literature on the utility of surgical resection for high grade glioma reveals that some medical academic genealogies tend to produce results which differ significantly from the medical literature as a whole. Articles written by these genealogies constitute a substantial portion of the literature.

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Table & Figure Legends

Table 1: Descriptive features of articles analyzed.

Table 2: Analysis of articles by medical academic genealogy

Table 3: Impact of key medical academic genealogies on publication results

Figure 1: Authors from the Berger (left) and Phillips (right) lineages. Larger node sizes indicate that the authors wrote a greater number of articles. Authors are colored green if all articles authored since founding or joining the lineage support maximal resection, yellow if over half support maximal resection, orange if less than or equal to half support maximal resection, and red if none support maximal resection. *(note to reviewer - see Figure1.pdf*

Table 1: Descriptive features of articles analyzed

	Results supportive of maximal resection		Results not supportive of maximal resection		All articles	
	n (%row)	**mean (sd)**	**n (%row)**	**mean (sd)**	**n (%all)**	**mean (sd)**
Articles (105 total)						
Total number of articles	76 (70%)		32 (30%)		108 (100%)	
Year of publication (range 1983-2014)						
Year of publication	76 (70%)	2008 (6.9)	32 (30%)	1998 (8.5)	108 (100%)	2005 (8.5)
Published before 2010	36 (58%)	2002 (6.4)	26 (42%)	1995 (6.6)	62 (57%)	1999 (7.2)
Published during or after 2010	40 (87%)	2013 (1.3)	6 (13%)	2011 (0.8)	46 (43%)	2012 (1.4)
Article sample size (range 19-40,137)						
Number of patients studied	76 (70%)	1875 (6279)	32 (30%)	121 (80)		1356 (5317)
Base 10 log, number of patients	76 (70%)	2.39 (0.71)	32 (30%)	1.98 (0.32)		2.27 (0.65)
Co-authors per article who are key authors†						
Mean number of authors per article	76 (70%)	3.23 (1.39)	32 (30%)	3.63 (1.91)	108 (100%)	3.35 (1.57)
Articles with at least one key author† who						
Is a neurosurgeon	52 (74%)		18 (26%)		70 (65%)‡	
Is a medical oncologist	29 (69%)		13 (31%)		42 (39%)‡	
Is a radiation oncologist	24 (56%)		19 (44%)		43 (40%)‡	
Is a member of another specialty	35 (73%)		13 (27%)		48 (44%)‡	
Joint first or last authorship						
Articles with joint first authorship	8 (89%)		1 (11%)		9 (8%)	
Articles with joint last authorship	2 (100%)		0 (30%)		2 (2%)	

†Key authors are authors who appear in a first or last author on any article studied

‡Key authors from multiple specialties collaborate on the same article, therefore values do not sum to 100%

Table 2: Analysis article results by medical academic genealogy

	Univariate models	Literature Controls +			Multivariate model	LASSO model
		Berger genealogy authorship	Phillips genealogy authorship	Radiation oncology authorship		
Parameter						
Known literature covariates						
Published during / after 2010	1.71 ***	NS	1.09 **	1.14 **	NS	NS
Article's sample size (log transformed)	1.56 ***	1.20 ***	1.41 **	1.29 **	1.28 **	1.28 **
Medical training genealogy						
Berger lineage (14 neurosurgeons)	2.76 ***‡	2.20 **	--	--	2.03 ○	2.04 ○
Phillips lineage (8 radiation oncologists)	-1.70 ***‡	--	-1.54 **	--	-1.32 ○	-1.35 **
Seven other lineages	NS	--	--	--	--	--
Specialty						
Any neurosurgeon key author	NS	--	--	--	--	--
Any medical oncologist key author	NS	--	--	--	--	--
Any radiation oncologist key author	-1.14 ***†	--	--	NS	NS	--
Any member of another specialty / non MD	NS	--	--	--	--	--

†Holm-Bonferroni correction for 4 comparisons
‡Holm-Bonferroni correction for 9 comparisons
NS: not significant, *** $p<0.01$, ** $p<0.05$, ○ $p<0.10$

Table 3: Impact of key medical academic genealogies on publication results

	Number of authors (% of dataset)	Number of unique articles (% of dataset)	Number of articles supporting maximal resection	Number of articles not supporting maximal resection
Identified medical training genealogies†				
Berger genealogy (neurosurgery)	14 (9%)	27 (25%)	26	1
Phillips genealogy (radiation oncology)	8 (5%)	14 (13%)	5	9
Both genealogies	22 (14%)	41 (38%)		

†See Figure 1 for genealogy membership