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Review Article

Mapping the connections between education and the risk of dementia

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Abstract

Many studies have shown a connection between education and late-life cognition, with the risk of dementia being inversely associated with educational attainment. This brief article proposes pathways through which cognitive ability in early life, subsequently reinforced by education and then by higher socioeconomic position in midlife, could confer a protective effect on cognitive decline many decades later, in late life. Taking a systems perspective, the article describes mutually reinforcing processes that operate to maintain the stability of cognitive abilities across the life course. The conclusion is that population-level interventions could be designed to enhance cognitive resiliency in our aging populations.

Introduction

Among many other studies [1-5], our Canadian Study of Health and Aging showed a relationship between educational attainment and dementia [6]. In addition to showing a gradient of dementia risk across educational levels, the study showed a contrast in the pattern of cognitive decline over time. While people with lower educational attainment who developed dementia showed a steady decline in cognitive test scores, more educated people maintained their scores for longer, then declined rapidly towards the end of their life – metaphorically falling off a cliff rather than sliding down a slope. A common interpretation is that educational level contributes to cognitive reserve which enables people to compensate for the brain pathology that underlies cognitive decline [7-10]. Cognitive reserve may reduce the risk of developing a pathology, or help a person compensate for the early stages of cognitive loss and delay the clinical expression of underlying pathology [11,12]. Indeed, Alzheimer's pathology has been found on autopsy in some people who did not demonstrate cognitive impairment *ante mortem*, and such cases typically occur among those with more education and whose jobs involved more complexity [6,8,13].

So, how may cognitive reserve be related to educational attainment? What are the origins of cognitive resiliency? Education, of course, is but one facet of socioeconomic position, and other social and economic influences will interact with that of education; a basic conceptual model was shown by Sharp and Gatz [4]. The current discussion describes in more detail some conceptual perspectives on hypothesized connections between education and eventual dementia across three life stages: processes that originate in early life, are maintained through middle age, and affect cognition in old age.

Early life

A striking finding of the Nun Study was the demonstration that the foundation stones of late-life cognition are laid very early in life [14-16], a finding reiterated by others [17,18]. Tracing this story back to the prenatal period, the developmental origins of health and disease (DOHaD) hypothesis shows how influences *in utero* have profound effects on the developmental

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trajectories of the child [19,20]. Maternal undernutrition during pregnancy triggers epigenetic mechanisms whereby the fetus redirects its development from stature to protect brain development. Gluckman applied the concept of predictive adaptation to describe how the developing organism senses its environment and adjusts its development to match this, better equipping it to survive in the environment into which it is likely to be born [21]. "Brain development is directed by genes but sculpted by experiences, particularly by those occurring during early sensitive or critical periods."[22] Brain plasticity is greatest in infancy and this underpins the lasting impact of early experiences: "Neural circuits are molded in early life to best represent the sensory input arriving at the time, and then eventually become hard-wired."[23] Thus, environmental and socioeconomic circumstances during pregnancy (established indirectly by the parents' education) influence the newborn's inherent cognitive capacity, circumstances that continue to affect cognitive development during the preschool years. The child's cognitive capacity then affects their school success in a process that is modified by parental support and attitudes toward learning, the quality of schooling, and other environmental influences, as sketched in (Figure 1).

The translation of innate mental capacity into school success is guided by the young child's environment; this is strongly related to socioeconomic status, and to the parents' attitudes towards education and learning, filtered through their parenting styles. For example, McEwen compared parenting styles across social classes. A middle-class parenting style of 'concerted cultivation' supports structured activities for the child and emphasizes language development and reasoning skills. This contrasted with an approach more common in working-class families of 'natural growth', which leaves children largely to explore ideas on their own, under parental regulation rather than discussion or negotiation [24]. In addition, wealthier parents commonly have the resources to travel with their children, to read to them, and to support the child's success in school [25]. Correspondingly, the children of more educated parents will have a larger vocabulary when they reach school age. Hart and Risley compared the number of words that children from disadvantaged versus professional families would hear at home during their first three years of life [26]. They estimated that children from professional families would hear 215,000 words each week, versus 125,000 for those in working-class families, and 62,000 words in welfare families. By their third birthday, children from professional families had an average vocabulary of 1,100 words; those from a working-class background knew 800 words, while the welfare children had 550 words. And these disparities endure: vocabulary skill at age three was strongly predictive of language skills at ages 9 to 10. Combining these parenting styles and vocabulary findings, Hart and Risley recorded the ratio of encouraging to discouraging words or prohibitions made by the parents. Children in professional families received an average of 32 affirmatives and 5 prohibitions per hour; for working-class families it was 12 affirmatives and 7 prohibitions; for the welfare children, it was 5 affirmatives and 11 prohibitions. This will plausibly have an invisible effect on the child's confidence, the feeling of agency, and motivation to explore, try new things, and pursue new ideas.

The British Millennium cohort study illustrated the strong socioeconomic gradients that exist in early cognitive development. The gradient for children at age 5 was attributed

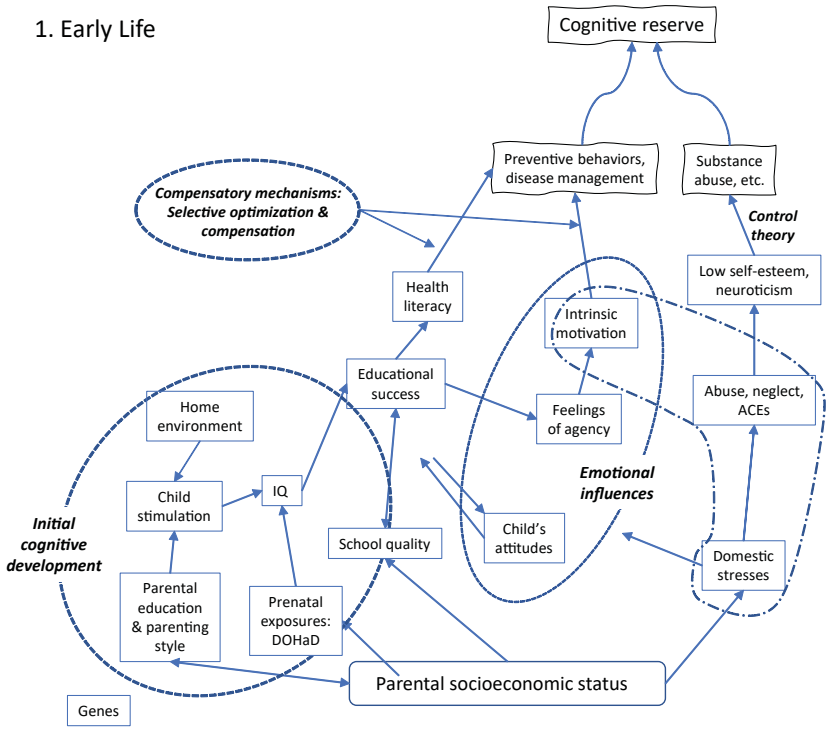

Figure 1: Conceptual model of influences on a child's developing cognitive capacity through infancy and childhood. (DOHaD: Developmental Origins of Health and Disease; IQ: Intelligence Quotient).

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in part to the early childhood caring environment, including the nature of family interactions, parenting styles, childcare arrangements, and home learning resources [27]. A child's cognitive ability is also influenced by that of the parents, which was shown in one study to explain one-sixth of the SES differential in cognitive ability, after adjustment for a wide set of demographic and behavioral factors, including attitudes toward education [28]. This analysis illustrated the remarkable variety of interacting influences. Decomposing the SES gradient in child cognitive test scores at age 10, parental cognitive ability explained 16%; the child's behaviors explained 10% and their attitudes toward education explained 20%; family background explained 12% and the social skills of parent and child explained 19% [28]. All of these factors interact and influence each other, as suggested in (Figure 1). Thus, the early life environment establishes both cognitive abilities and motivation to succeed in education; the child's attitude toward education strongly predicts school success and is reinforced by success [29]. Whether positive or negative, the child's attitudes also reflect the opinions and abilities of the parents, reinforcing intergenerational patterns of educational attainment and thereby socioeconomic status – a finding replicated in the Uppsala Multigenerational Birth Cohort Study [30].

Transition to adulthood

Cognitive ability in adolescence lays a foundation stone for adult social position which ultimately influences a person's health in later life; adulthood forms a time for consolidating, broadening, and reinforcing cognitive resiliency. Schulz and Heckhausen summarized many of the mechanisms in a conceptual model of the requirements for successful adaptation to challenges across the lifespan [31-34]. Their model holds that four principles underpin optimal human development, and these shed light on possible connections between educational attainment and late-life cognition. First, a child's environment must offer a diversity of opportunities for exploring different options and for developing a repertoire of skills – the type of childhood context available to those in higher socioeconomic positions. Diversity in early experiences provides raw materials for cognitive development. Second, this diversity should be balanced against selectivity, to establish a field of expertise and establish a developmental path that matches the person's capacities and environment. However, the freedom to explore and test options is unavailable to most people living in disadvantaged circumstances, yet such autonomy has been linked to cognitive resiliency [35]. Third, the individual must learn to cope with failures encountered along the way and to compensate for these. Finally, the individual must learn to manage the trade-offs across the domains of life, recognizing that time is limited and that one cannot do everything one wishes. Baltes and Baltes built on Schulz and Heckhausen's four principles in their theory of selective optimization with compensation [36]. Selection refers to choosing life paths carefully, while compensation refers to the ability to handle failures that occur.

Control theory assumes that humans seek to exert control over their environment throughout their life span [31] and the level of control is strongly predicted by educational and broader social status. Primary control refers to the young person's efforts to control the external world around them, whereas secondary control refers to control over how they adapt to that environment. Control involves cognitive and behavioral components, although primary control predominantly involves action whereas secondary control is largely cognitive. Secondary control develops as the young adult learns to deal with success and failure, with acceptance and rejection. This links to selective optimization because, as the adolescent becomes more focused and selective in his or her activities, the sense of primary control increases as they choose areas of greatest reward – and their repertoire of choices reflects their educational attainment.

Influences in middle age

The life course of adulthood presents a series of branches on the road toward maintaining and further developing cognitive capacities, branches that are notably influenced by a person's educational level and consequent socioeconomic position in industrialized societies. A central branching point is seen in a person's occupational path, which reflects education and training, with options spanning a spectrum from cognitively stimulating and physically safe activities to stultifying and potentially hazardous occupations. The combined influences of the many facets of an occupational setting have been described in terms of the 'worksome'. (The '-ome' and '-omics' suffixes refer to studying the functioning of an entire, complex entity: genomics refers to the joint operation of all our genes rather than a particular one.) Whereas environmental epidemiology traditionally studies the effect of a specific exposure on a particular disease, the 'exposome' forms an ambitious proposal to document as complete a history as possible of a person's cumulated exposures to summarize how the environment influences health and disease [37]. Eyles, et al. applied this notion to summarize the impact of work settings on a person's physical and mental health, cumulating over their work history, and ultimately influenced by their educational status [38]. The worksome portrays influences in a system of concentric influences, beginning with national, and then local factors affecting work, such as unemployment rates and pay scales. Within this context, it focuses on the characteristics of particular workplaces, considering job security, support from colleagues, stressfulness, and level of mental stimulation (see the center of Figure 2). Physical characteristics of work include occupational exposures for some that could be cognitively damaging, such as exposure to neurotoxins. Work characteristics interact with the person's lifestyle and non-work choices and with their biological characteristics such as age, existing health problems, and their motivation to maintain their health. These factors, also, are partially influenced by education via the concepts of health literacy and motivation as sketched on the left of (Figure 2).

So how might a person's occupation affect cognition? Work can stimulate or stultify. Hyun, et al. identified both independent and overlapping influences of education and occupational complexity on the risk of dementia [3] and a person's vocation may confer mental resiliency [39]. Siegrist's

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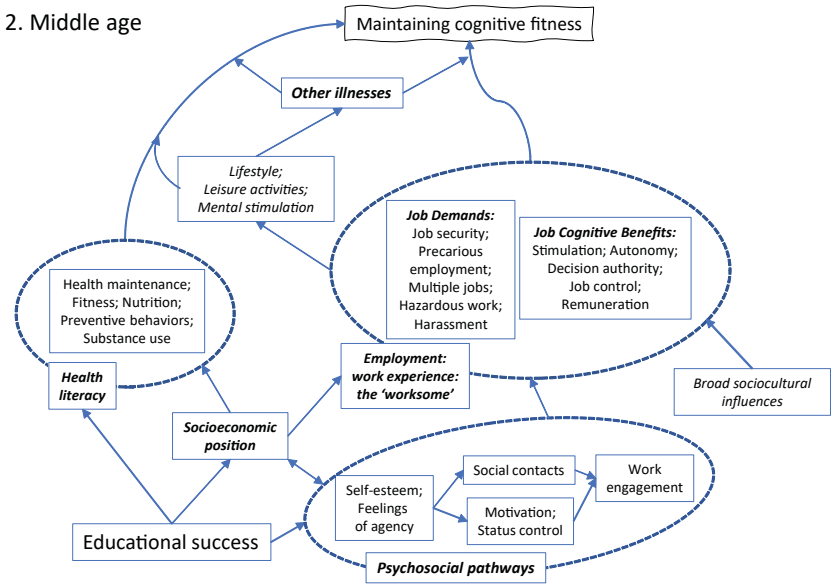

Figure 2: Summary of possible pathways linking education with the maintenance of cognitive capacity during adulthood. The curved arrows suggest indirect influences, in which other factors play a role.

effort-reward imbalance model suggested ways in which an occupation may be stressful or stimulating [40]. For example, the notion of being 'in flow' describes tasks that are challenging but whose goals are clear, and the person feels rewarded and motivated to strive for success, stretching and then rewarding their creativity [41]. But when high effort is not matched by commensurate rewards an imbalance arises, and this effort-reward imbalance causes emotional distress, strain, autonomic arousal, and inflammation [40,42]. Note that the relationship is typically not linear: excessive challenge may overwhelm rather than strengthen, perhaps shedding light on the cognitive fates of Ronald Reagan or Margaret Thatcher. Nor is the relationship between stimulation and mental preservation simply mechanical: a modifying influence is the worker's intrinsic motivation to succeed in a challenging situation. Intrinsic motivation includes conscientiousness, a drive to succeed, and the feeling of reward in rising to a challenge; less positively it may also include over-commitment, in which people underestimate work demands and exaggerate their capacities [43]. Siegrist spoke of status control, referring to a person's subjective sense of being in control of their social standing, linked to internal feelings of mastery, self-efficacy, and esteem [40], forming one of the psychosocial pathways in (Figure 2). On the negative side, various job characteristics may reduce status control: job insecurity, changes made without consulting employees, low prospects for promotion, or when the worker feels underqualified for their job. A balance between the person's capacity and their challenge is critical in steadily building mental resiliency; low-status control threatens the worker's trust and leads to a sense of unfairness termed 'imbalance' and feelings of stress.

Education also influences the person's non-work activities in adulthood, summarized in (Figure 2) via the concepts of health literacy and lifestyle. Research shows protective effects of lifestyle choices such as exercise, not smoking, and limiting alcohol consumption, each associated with the preservation of cognitive function [12], as sketched on the left of (Figure 2). Lifestyle is also shown as influencing cognition indirectly, by increasing the risk of a range of vascular and other conditions that can compromise cognitive function in later life. Such illnesses are shown as effect modifiers in the Figure. Once sick, low education, through its connection with income, affects a person's access to health insurance and health services, and their ability to afford medications.

Cognition in later life

Like physical capacities, cognitive abilities decline naturally with age and require effort to maintain. Hypothesized ingredients in the pathway between education and late-life cognition are traced in (Figure 3). Conservation of resources theory describes how humans follow a fundamental drive to protect their integrity, to retain their current resources – whether possessions, skills, energy, or capacities [44]. Within this basic motivation, socioeconomic resources will influence the aging person's ability to retain their cognitive abilities. Returning to the theory of control, primary control declines with retirement and advancing age. Secondary control then becomes more salient and guides the person in handling their loss of capacity, and in maintaining self-esteem and motivation. Heckhausen proposed a 'lines-of-defense' model to propose how people adjust to physical and mental decline via cycles of engaging in new goals while disengaging from others; their success in achieving this redirection reflects educational and social standing [32,34]. The theory of selective optimization with compensation offers an alternative description [36]. Baltes and Baltes argued that as people age and lose cognitive and physical abilities they find ways to cope with and compensate for the losses and to optimize their use of those abilities they still retain [36]. Here, cognitive reserve that was built in childhood and maintained through the midlife period contributes directly to this process. Their

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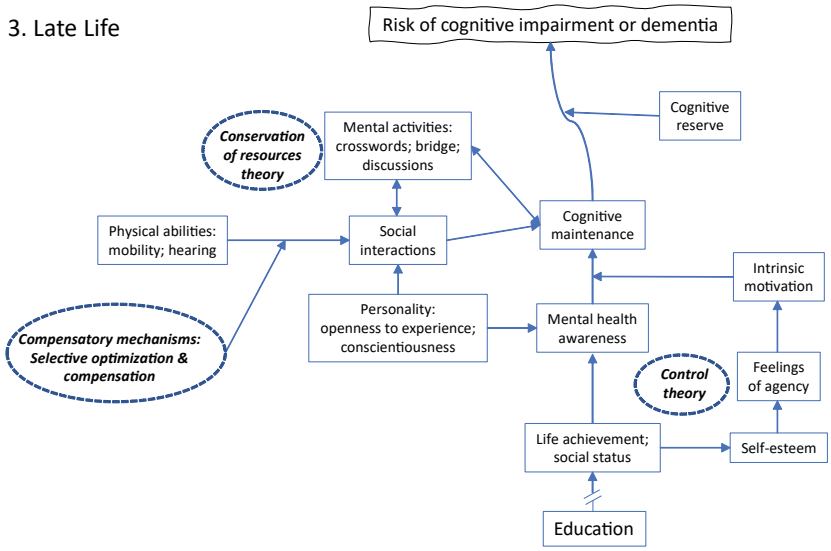

Figure 3: Conceptual model of influences in older age that modify the connection between early life education and ultimate risk of cognitive impairment.

creativity and resources affect the ways they can compensate for cognitive decline and maintain independence, for example by having access to a caregiver or by using mechanical devices. These are more available to those in higher educational and socioeconomic groups.

Conclusion

Educational attainment has been associated with late-life dementia in many, but by no means all, studies. Among the former, dementia incidence risk ratios comparing those with low versus high educational levels range from roughly 2 to 4. The present argument is that so many processes intervene between early life cognitive ability and ability decades later at the end of life that it is not surprising that some studies have found little or no association between the two. If a study were able to take a fuller, life course perspective and adjust for countervailing influences, exceptions to the rule could be explained and the true relationship might be found to be stronger.

Given the philosophy that it is more efficient to prevent than to treat and given the current limited success of treatments for late-life cognitive loss, it becomes important to understand not only what factors influence cognitive impairments, but how and why. It is deeply unsettling that our dementia risk may be largely established very early in life. This should pave the way to proposing strategies, beginning in early life and continuing through middle age, to modify or at least counteract cognitive risk factors. While many epidemiological studies have identified particular predictors of cognitive loss, it is important to recognize that multiple factors are involved in any causal process and that these factors interact and mutually influence each other (positively or negatively) over time. This means that interventions to modify a single factor may be blocked (but may also be supported) by other influences, operating as a system. Numerous studies have characterized families whose children are at elevated risk of poor educational outcomes; early interventions can and must continue to support those children.

The exposome perspective then supports continued attention to the cognitive environment of people as they join the workforce and through their subsequent life course. Opportunities abound. The ubiquity of smartphones offers avenues for both cognitive and social engagement applications designed to foster cognitive resiliency, the housing environment and transport systems for elderly people must bear in mind the importance of creating and retaining social ties and mentally stimulating activities, of whatever type the person prefers. There seems little reason, for example, why television programs could not become more interactive: use the remote control to participate in an online opinion poll of who committed the murder, or whether the person will be found guilty before all is revealed at the end of the program. The rising tide of dementia has made finding ways to foster cognitive resiliency at the population level a major priority. Figures 2,3 above sketch many variables that offer potential pressure points for such interventions.

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