

Obesity interacts with infectious mononucleosis in risk of multiple sclerosis

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Background and purpose: The possible interaction between adolescent obesity and past infectious mononucleosis (IM) was investigated with regard to multiple sclerosis (MS) risk.

Methods: This report is based on two population-based case-control studies, one with incident cases (1780 cases, 3885 controls) and one with prevalent cases (4502 cases, 4039 controls). Subjects were categorized based on adolescent body mass index (BMI) and past IM and compared with regard to occurrence of MS by calculating odds ratios with 95% confidence intervals (CIs) employing logistic regression. A potential interaction between adolescent BMI and past IM was evaluated by calculating the attributable proportion due to interaction.

Results: Regardless of human leukocyte antigen (HLA) status, a substantial interaction was observed between adolescent obesity and past IM with regard to MS risk. The interaction was most evident when IM after the age of 10 was considered (attributable proportion due to interaction 0.8, 95% CI 0.6–1.0 in the incident study, and attributable proportion due to interaction 0.7, 95% CI 0.5–1.0 in the prevalent study). In the incident study, the odds ratio of MS was 14.7 (95% CI 5.9–36.6) amongst subjects with adolescent obesity and past IM after the age of 10, compared with subjects with none of these exposures. The corresponding odds ratio in the prevalent study was 13.2 (95% CI 5.2–33.6).

Conclusions: An obese state both impacts the cellular immune response to infections and induces a state of chronic immune-mediated inflammation which may contribute to explain our finding of an interaction between adolescent BMI and past IM. Measures taken against adolescent obesity may thus be a preventive strategy against MS.

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease that develops as a result of a complex interplay between genetic and environmental/lifestyle factors. As in most autoimmune disorders, the strongest genetic associations with MS are located within the human leukocyte antigen (HLA) complex. The class II allele HLA-DRB1*15 increases the risk of developing MS in almost all populations, with an odds ratio

around 3 [1], whereas the class I allele HLA-A*02 has a protective effect with an odds ratio of approximately 0.7 [2,3].

Established environmental risk factors influencing MS risk are smoking [4], sun exposure habits/vitamin D status [5] and a history of infectious mononucleosis (IM) [6]. Furthermore, high body mass index (BMI) at a young age has repeatedly been associated with increased risk of developing MS [7–10] and a number of other autoimmune disorders [11]. Leptin, which is produced mainly by adipose tissue in proportion to body fat mass, has been considered a link between obesity and autoimmunity, promoting the onset and progression of autoimmune responses by switching

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the phenotype towards a Th1 response [12]. Obesity also results in a state of immunodeficiency which may alter the way a pathogen induces an immune response [13]. Using two Swedish population-based case-control studies, the impact of IM on MS risk and the potential interaction between adolescent obesity and past IM was investigated. Since HLA MS risk genes interact with both adolescent obesity [14] and increased EBNA1 levels [15] with regard to MS risk, HLA genotype was also taken into consideration.

Methods

Study design and study subjects

This study was based on two independent population-based, case-control studies on environmental and genetic risk factors for MS, termed Epidemiological Investigation of Multiple Sclerosis (EIMS) and Genes and Environment in Multiple Sclerosis (GEMS). In EIMS, incident cases of MS were recruited via 40 study centres, including all university hospitals in Sweden. Cases were diagnosed by a neurologist according to the McDonald criteria [16]. For each case, two controls were randomly selected from the national population register, frequency matched by age (5-year age groups), gender and residential area. The study period was April 2005 to September 2012.

In GEMS, prevalent cases of MS, distinct from those in EIMS, were identified from the Swedish national MS registry during 2009 and 2010. For each case, one control was randomly selected from the national population register matched for age, gender and residential area at the time of disease onset. All cases in both studies fulfilled the McDonald criteria [16]. Ethical approval for both EIMS and GEMS was obtained from the relevant ethics committees. More details on study design and methods are given elsewhere [4].

Data collection

In both studies, information regarding lifestyle factors and different exposures amongst cases and controls was collected using a standardized questionnaire. In EIMS, the questionnaire was given to the cases shortly after they had received their diagnosis and was sent by mail to the controls. In GEMS, the questionnaire was sent by mail to all participants. All questionnaires were supposed to be answered at home. In EIMS, incompletely answered questionnaires were completed by mail or by telephone. Participants were asked whether they had ever had IM and, if yes, at what age the infection occurred. For each case in both studies, the time of the initial appearance of MS

symptoms was used as an estimate of the disease onset, and the year in which this occurred was defined as the index year. The corresponding controls were given the same index year. IM was only considered prior to the index year.

Information was obtained regarding current body height and body weight at age 20. Using current height, BMI was calculated at age 20 by dividing weight in kilograms by height in meters squared. As in our previous paper on BMI and MS [14], subjects with BMI exceeding 27 kg/m² were defined as obese. In order to get more information on obesity before the age of 20, a complementary question regarding childhood obesity was sent to all EIMS participants in 2013. Participants were asked to select one of nine body silhouettes, ranging from very thin to extremely obese, that best represented their body size at age 10. Those with silhouettes 5 and 6 were classified as overweight, and those with silhouettes 7–9 as obese.

In EIMS, main questionnaires were obtained from 1935 cases and 4216 controls, the response proportion being 91% for the cases and 69% for the controls. Subjects younger than 20 at the time of the index year or those with missing data on prior IM were excluded (155 cases and 331 controls). With a response proportion of 82% for the cases and 66% for the controls, the GEMS material comprises 5129 prevalent MS cases and 4509 controls. Of these, 627 cases and 470 controls were excluded due to missing data on BMI at age 20 or prior IM.

Genotyping and definition of genetic risk factors

All EIMS participants who filled out the questionnaire were asked to provide a blood sample. Blood samples were available for 89% of the cases and 56% of the controls. Allelic dosage of HLA-DRB1*15 and HLA-A*02 were obtained by either polymerase chain reaction amplification with sequence-specific primers, single-nucleotide polymorphism imputation or TaqMan allelic discrimination as previously described [14].

The study subjects were classified according to carriage of HLA-DRB1*15 alleles (any versus none). The HLA-A*02 allele has reproducibly shown a protective association to MS. Absence of HLA-A*02 is thus a risk factor of developing the disease, and the participants were classified according to carriage of any HLA-A*02 allele versus no carriage.

Statistical analysis

Using logistic regression, the impact of prior IM on MS risk amongst subjects who did and did not report adolescent obesity was investigated by calculating the

odds ratio together with 95% confidence interval (CI). The potential interaction between adolescent obesity and prior IM was analysed using departure from additivity of effects as the criterion of interaction and was evaluated by calculating the attributable proportion due to interaction (AP) together with a 95% CI. AP is the proportion of the incidence amongst individuals exposed to two interacting factors that is attributable to the interaction *per se*; thus an AP >0 indicates presence of interaction. As a complement, the relative excess risk due to interaction and the synergy index were also calculated together with 95% confidence interval [17].

Since the two most important genetic MS risk factors (presence of HLA-DRB1*15 and absence of HLA-A*02) interact with both adolescent obesity and prior IM with regard to MS risk [14,15], analysis of the interaction between adolescent obesity and prior IM was also carried out in EIMS, limited to HLA-DRB1*15 negative subjects adjusted for HLA-A*02 status, where these data were available.

Matched analyses were performed based on all available case-control duplets/triplets, as well as unmatched analyses of the data based on all available cases and controls. Only the results from the unmatched analyses are presented in this report since these were in close agreement with those from the matched analyses but in general had a higher degree of precision (due to a higher number of controls).

All analyses were adjusted for age, gender, residential area, ancestry and smoking. Assessment of ancestry was based on whether the subject was born in Sweden or not, and whether either of the subject's parents had immigrated to Sweden. A subject who was born in Sweden, whose parents had not immigrated, was classified as Swedish. Smoking was dichotomized into ever or never smokers. Adjustments were also made for heredity (having or not having a first or second degree relative with MS), educational level, socioeconomic status, snuff use (yes/no), sun exposure habits and vitamin D status (more or less than 50 ng/ml or unknown), but these factors had a minor influence on the results and were not retained in the final analyses. Educational level was categorized into no post-secondary education, post-secondary education without a university degree, or university degree. The last occupation during the year before the index year was used as a marker for socioeconomic class which was categorized into the following strata: (i) workers in goods production; (ii) workers in service production; (iii) employees at lower and intermediate levels; (iv) employees at higher levels, executives, university graduates; and (v) others such as pensioners, students and unemployed. Based on three questions regarding

exposure to ultraviolet radiation where each answer alternative was given a number ranging from 1 (the lowest exposure) to 4 (the highest exposure), an index was constructed by adding the numbers together and thus acquired a value between 3 and 12 [5]. Ultraviolet radiation exposure was then dichotomized into high or low exposure (index value more or less than 6). All analyses were conducted using Statistical Analysis System (SAS) version 9.2; SAS Institute Inc., Cary, NC, USA.

Results

Our analyses of adolescent obesity and past IM with regard to MS risk included 1780 cases and 3885 controls from EIMS and 4502 cases and 4039 controls from GEMS. Amongst the cases, the mean age at disease onset was 34.2 years in EIMS and 33.2 years in GEMS. The majority of cases in EIMS were recruited within 1 year after the diagnosis and the questionnaires were completed after a median of 2.0 years following the onset of the disease. In GEMS, the median duration from disease onset to inclusion in the study was 17.0 years. All cases in both studies fulfilled the McDonald criteria [16]. Selected characteristics of cases and controls are presented in Table 1. Of the subjects who answered the complementary question and were defined as obese in EIMS (at age 20), 63% of the cases and 58% of the controls also reported childhood overweight or obesity.

In both EIMS and GEMS, the risk of MS associated with past IM was significantly higher amongst subjects with adolescent obesity (Table 2). In both studies, a significant interaction was observed between adolescent obesity and past IM with regard to MS risk (Table 3). The interaction was more pronounced when IM after the age of 10 was considered (AP 0.8, 95% CI 0.6–1.0 in EIMS; AP 0.7, 95% CI 0.5–1.0 in GEMS). Compared with non-obese subjects with no history of IM, the odds ratio of MS amongst subjects with adolescent obesity and IM after age 10 was 14.7 (95% CI 5.9–36.6) in EIMS and 9.3 (95% CI 3.3–26.1) in GEMS. The interaction was evident also in the absence of the HLA-DRB1*15 risk allele (Table 4).

To shed light on whether the temporal relation between obesity and IM affected the results, additional analyses were performed. Few subjects reported IM after the age of 20 (48 cases and 69 controls in EIMS, and 126 cases and 79 controls in GEMS). A strong interaction between adolescent obesity and IM after age 20 was observed in EIMS (AP 0.9, 95% CI 0.7–0.9). However, it was not possible to perform the corresponding analysis in GEMS since no controls reported the combination of adolescent obesity and

Table 1 Characteristics of cases and controls in EIMS and GEMS

	EIMS		GEMS	
	Cases	Controls	Cases	Controls
Women (<i>n</i> , %)	1295 (73)	2838 (73)	3330 (74)	3056 (76)
Men (<i>n</i> , %)	485 (27)	1047 (27)	1172 (26)	983 (24)
Swedish origin (<i>n</i> , %)	1411 (79)	2938 (76)	3698 (82)	3300 (82)
IM (<i>n</i> , %)	326 (18)	421 (11)	662 (15)	313 (8)
Prepubescent IM	115	19	188	95
IM before age 20	278	352	536	234
IM at or after age 20	48	69	126	79
Mean age (SD)	15 (6)	16 (7)	18 (13)	17 (13)
Median age	15	16	15	15
Range of ages	1–41	1–52	0–30	0–27
Smoking (<i>n</i> , %)	936 (53)	1747 (45)	2589 (58)	1979 (49)
Large conurbations (<i>n</i> , %)	465 (26)	974 (25)	2153 (48)	1912 (47)
Snuff use (<i>n</i> , %)	280 (16)	613 (16)	431 (10)	370 (9)
BMI > 27 kg/m ² (<i>n</i> , %)	166 (9)	201 (5)	240 (5)	159 (4)
Total (<i>n</i> , %)	1780 (100)	3885 (100)	4502 (100)	4039 (100)

IM, infectious mononucleosis; BMI, body mass index.

Table 2 Odds ratio (OR) with 95% confidence interval (CI) of developing multiple sclerosis for subjects with a reported history of infectious mononucleosis, based on EIMS and GEMS data, and limited to HLA-DRB1*15 negative subjects in EIMS

	EIMS				GEMS				
	ca/co ^a	OR (95% CI) ^c	OR (95% CI) ^d	<i>P</i>	ca/co ^b	OR (95% CI) ^c	ca/co ^a	OR (95% CI) ^b	<i>P</i>
Total	326/421	1.9 (1.6–2.2)	1.9 (1.6–2.3)	<0.0001	172/361	1.9 (1.6–2.3)	615/314	1.9 (1.6–2.2)	<0.0001
Women	246/322	1.8 (1.5–2.2)	1.9 (1.5–2.4)	<0.0001	126/275	1.8 (1.5–2.3)	472/254	1.8 (1.6–2.2)	<0.0001
Men	80/99	1.9 (1.4–2.7)	2.0 (1.3–3.1)	<0.0001	46/86	2.2 (1.5–3.3)	143/60	2.1 (1.6–2.9)	<0.0001
BMI < 27	289/407	1.8 (1.5–2.1)	1.8 (1.4–2.2)	<0.0001	149/347	1.8 (1.4–2.2)	574/307	1.8 (1.6–2.1)	<0.0001
BMI > 27	37/14	3.7 (1.9–7.3)	6.9 (2.4–19.8)	0.0002	23/14	4.1 (1.9–9.1)	41/7	4.1 (1.8–9.3)	0.0009

BMI, body mass index.

^aNumber of exposed cases and controls. ^bAdjusted for matching variables, origin, smoking habits, HLA-DRB1*15 and HLA-A*02. ^cNumber of HLA-DRB1*15 negative cases and controls. ^dAdjusted for matching variables, origin and smoking habits. ^eAdjusted for matching variables, origin, smoking habits and HLA-A*02.

IM after age 20. Analyses in EIMS were further performed in which obesity was defined differently [obese at age 10 but not at age 20 (group 1), obese at age 20 but not at age 10 (group 2) and obese both at age 10 and at 20 (group 3)]. The interaction between obesity and past IM was significant in all groups (AP 0.6, 95% CI 0.3–0.7 in group 1; AP 0.8, 95% CI 0.4–0.8 in group 2; and AP 0.9, 95% CI 0.2–1.1 in group 3) (not shown in the table).

Discussion

According to our findings, a substantial interaction takes place between adolescent obesity and past IM with regard to risk of developing MS. Both adolescent obesity and increased EBNA1 levels have been observed to interact with HLA genotype in the development of MS [14,15], and our finding of an interaction between established environmental risk factors further adds to the complexity of disease susceptibility.

Our finding emphasizes the need to take both genotype and environmental exposures into consideration when investigating the impact of specific risk factors on MS risk.

Obesity induces a state of chronic, low-grade inflammation that arises from the production and secretion of inflammatory mediators driven by adipose tissue macrophages [18]. Leptin, produced mainly by adipose tissue in proportion to body fat mass [19], promotes Th1 responses and decreases the function of regulatory T-cells that are capable of suppressing immune responses. The reduced suppressive function of regulatory T-cells has previously been reported in autoimmune diseases such as MS [20–23]. It has been suggested that leptin specifically impairs the proliferation of regulatory T-cells, thereby promoting the onset and progression of autoimmune responses [12,24–26]. Obesity has been associated with increased susceptibility to a number of inflammatory and autoimmune diseases including MS [11].

BMI > 27	IM	ca/co ^a	OR (95% CI) ^b	OR (95% CI) ^c	P
EIMS					
Past IM					
–	–	1325/3277	1.0 (–)	1.0 (–)	
+	–	129/187	1.7 (1.3–2.1)	1.7 (1.4–2.2)	<0.0001
–	+	289/407	1.8 (1.5–2.1)	1.8 (1.5–2.2)	<0.0001
+	+	37/14	6.6 (3.6–12.4)	8.1 (4.2–15.0)	<0.0001
Interaction term					
AP					
RERI					
SI					
IM after age 10					
–	–	1325/3277	1.0 (–)	1.0 (–)	
+	–	129/187	1.7 (1.3–2.1)	1.7 (1.4–2.2)	<0.0001
–	+	208/249	2.1 (1.7–2.6)	2.1 (1.7–2.6)	<0.0001
+	+	28/6	12.0 (4.9–29.1)	14.7 (5.9–36.6)	<0.0001
Interaction term					
AP					
RERI					
SI					
GEMS					
Past IM					
–	–	3644/3574	1.0 (–)		
+	–	196/152	1.3 (1.0–1.6)		<0.0001
–	+	618/306	2.0 (1.7–2.3)		0.002
+	+	44/7	6.3 (2.8–13.9)		<0.0001
Interaction term ^d					
AP					
RERI					
SI					
IM after age 10					
–	–	3644/3574	1.0 (–)		
+	–	196/152	1.3 (1.0–1.6)		0.03
–	+	505/245	1.8 (1.8–2.4)		<0.0001
+	+	37/4	9.3 (3.3–26.1)		<0.0001
Interaction term					
AP					
RERI					
SI					

^aNumber of exposed cases and controls; ^badjusted for matching variables, origin and smoking habits; ^cadjusted for matching variables, origin, smoking habits, HLA-DRB1*15 and HLA-A*02; ^dindicates interaction on the multiplicative scale.

Table 3 Odds ratio (OR) with 95% confidence interval (CI) of developing multiple sclerosis for subjects with different combinations of adolescent body mass index (BMI) and infectious mononucleosis (IM) status. Attributable proportion due to interaction (AP), relative excess risk due to interaction (RERI) and synergy index (SI) for the interaction between adolescent BMI and past IM

However, obesity results in a state of immunodeficiency with decreased cytokine production, altered antigen presentation, and reduced macrophage and dendritic cell function [13]. Obesity-induced immunodeficiency may thus alter the way a pathogen induces an immune response and increase the risk of an inflammatory response directed at self-antigens. It is also possible that the immunodeficient state renders obese people more susceptible to infectious agents, which then trigger an autoimmune response.

Epstein–Barr virus (EBV) has been associated with increased risk of various autoimmune diseases, and several mechanisms have been suggested to explain the association [27]. The leading hypothesis is that the immune response to EBV infection in genetically susceptible individuals cross-reacts with self-antigens [28]. It has been suggested that CD8⁺ T-cell deficiency

underlies the development of autoimmune diseases by impairing CD8⁺ T-cell control of EBV infection, with the result that EBV-infected autoreactive B-cells accumulate in the target organ where they produce autoantibodies and provide co-stimulatory survival signals to autoreactive T-cells [27].

Epstein–Barr virus infection is asymptomatic in childhood but commonly manifests as IM when it is delayed to the time of adolescence or later. The absolute size of the CD8⁺ T-cell population normally declines threefold between the ages of 2 and 16 [29]. The age-related decline in CD8⁺ T-cells may contribute to explaining both the increased risk of MS associated with late EBV infection [27] and the greater impact of past IM on MS risk amongst obese subjects with deficiency of CD8⁺ T-cells [13] than amongst non-obese subjects. It may also contribute to explaining why the

Table 4 Odds ratio (OR) with 95% confidence interval (CI) of developing multiple sclerosis for subjects with different combinations of adolescent body mass index (BMI) and infectious mononucleosis (IM) status. HLA-DRB1*15 negative subjects. Attributable proportion due to interaction (AP), relative excess risk due to interaction (RERI) and synergy index (SI) for the interaction between adolescent BMI and past IM

BMI > 27	IM	ca/co ^a	OR (95% CI) ^b	OR (95% CI) ^c	P
EIMS					
Past IM					
-	-	688/2748	1.0 (-)	1.0 (-)	
+	-	66/163	1.6 (1.2-2.2)	1.6 (1.5-1.8)	0.002
-	+	149/347	1.7 (1.4-2.1)	1.8 (1.6-1.9)	<0.0001
+	+	23/14	6.9 (3.5-13.5)	7.0 (6.4-7.6)	<0.0001
Interaction term					
AP					
2.4 (1.1-5.1)					
RERI					
4.5 (1.1-11.2)					
SI					
4.3 (1.8-10.4)					
IM after age 10					
-	-	688/2748	1.0 (-)	1.0 (-)	
+	-	66/163	1.6 (1.2-2.2)	1.6 (1.2-2.2)	0.0002
-	+	103/213	2.0 (1.5-2.6)	2.0 (1.6-2.6)	<0.0001
+	+	18/6	13.1 (5.1-33.2)	13.2 (5.2-33.6)	<0.0001
Interaction term					
AP					
4.0 (1.5-11.0)					
RERI					
10.4 (2.5-30.5)					
SI					
7.4 (2.5-22.1)					

^aNumber of exposed cases and controls; ^badjusted for matching variables, origin and smoking habits; ^cadjusted for matching variables, origin, smoking habits and HLA-A*02.

interaction between adolescent obesity and past IM with regard to MS risk was more pronounced when IM after the age of 10 was considered.

Susceptibility to specific autoimmune diseases is conferred by specific alleles of HLA class I and II. The molecules encoded by the specific alleles determine which self-antigens are recognized by T-cells. Both HLA-DRB1*15 and HLA-A*02 have been observed to interact with adolescent obesity [14] as well as with EBNA1 titres [15]. In order to shed light on the influence from these genetic risk factors on the interaction between IM and adolescent obesity an analysis was performed restricted to HLA-DRB1*15 negative subjects where the signs of interaction were very similar to those for the whole material. It was not possible to perform the same analysis amongst HLA-DRB1*15 positive individuals since there were no controls in the comparison group (non-obese IM negative subjects).

Our analyses were adjusted for a broad range of potential confounding factors. Besides gender, residential area, ancestry and smoking, socioeconomic status, educational level, snuff use, sun exposure habits and vitamin D status were considered with regard to their potential confounding effects. Both obesity and deprivation of sunlight can lead to lower levels of vitamin D, and both deprivation of sunlight and vitamin D deficiency could aggravate the CD8+ T-cell deficiency and affect the immunological response to EBV infection [27]. However, adjustments for sun exposure habits during the 5 years preceding inclusion in the study did not affect our results, neither did adjustments for vitamin D status at inclusion in

the study. However, the possibility that low sun exposure or vitamin D deficiency at an early age affect the association between adolescent obesity and past IM cannot be ruled out.

The interaction between adolescent obesity and past IM was examined by calculation of departure from additivity of effects, described as the method most appropriate for identifying specific biological interactions. Two risk factors can either be independent (i.e. no pathway to disease requires the involvement of both risk factors) or have biological interaction (i.e. at least one pathway towards disease requires the involvement of both risk factors). Independent risk factors adhere to an additive model and interaction results in departure from additivity of the disease rates [17,30]. As a complement the investigated interactions on the multiplicative scale (by including an interaction term in the logistic model) were also calculated. All the reported interactions were statistically significant also on the multiplicative scale.

It is important to consider potential drawbacks, confounders or biases in our study. Both studies retrospectively gathered information regarding lifestyle factors and personal information such as weight and height. EIMS primarily included cases who had received the diagnosis within the past year in order to minimize recall bias. Moreover, the questionnaire contained a wide range of questions regarding many potential environmental risk factors and no section in the questionnaire was given prime focus. GEMS was based on prevalent cases of MS (mean duration of disease 17 years) and recall bias may therefore be

more substantial than in EIMS. However, a validation study amongst women in the Nurses' Health Study found high correlations between recalled and measured past weight. Participants slightly underreported weight at 18 years of age with a mean difference of 1.4 kg [31]. The underreporting of weight in our study probably does not differ between cases and controls, especially since there was virtually no association between current BMI and MS risk. There is an obvious risk of misclassification when categorizing the subjects into those with past IM and those with no history of IM. Subjects may unknowingly have had IM, and infection by other pathogens may cause an IM-like illness. However, the risk of MS amongst subjects with a reported past history of IM was in accordance with that of previous studies on past IM and MS risk [6].

Another concern is that the recruitment of cases and controls may introduce selection bias. Considering the structure of the public Swedish healthcare system, which provides equal free of charge access to medical services for all Swedish citizens, it is most likely that almost all cases of MS are referred to neurological units.

The proportion of respondents with regard to participation in EIMS was 91% for cases and 69% for controls. A potential selection bias may result from the relatively high proportion of non-responders amongst the controls. However, this bias is most likely to be modest because the prevalence of smoking amongst the controls, seen as an indicator of lifestyle, was in line with that of the general population at equivalent ages [32]. Furthermore, both the prevalence of drinkers amongst the controls and their drinking patterns were in line with those of the general population [32].

In conclusion, a substantial interaction between adolescent obesity and past IM with regard to MS risk was observed. The obese state both impacts the cellular immune response to infections and induces a state of chronic immune-mediated inflammation

which may contribute to explaining the interaction. Measures taken against adolescent obesity may thus be a preventive strategy against MS.

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