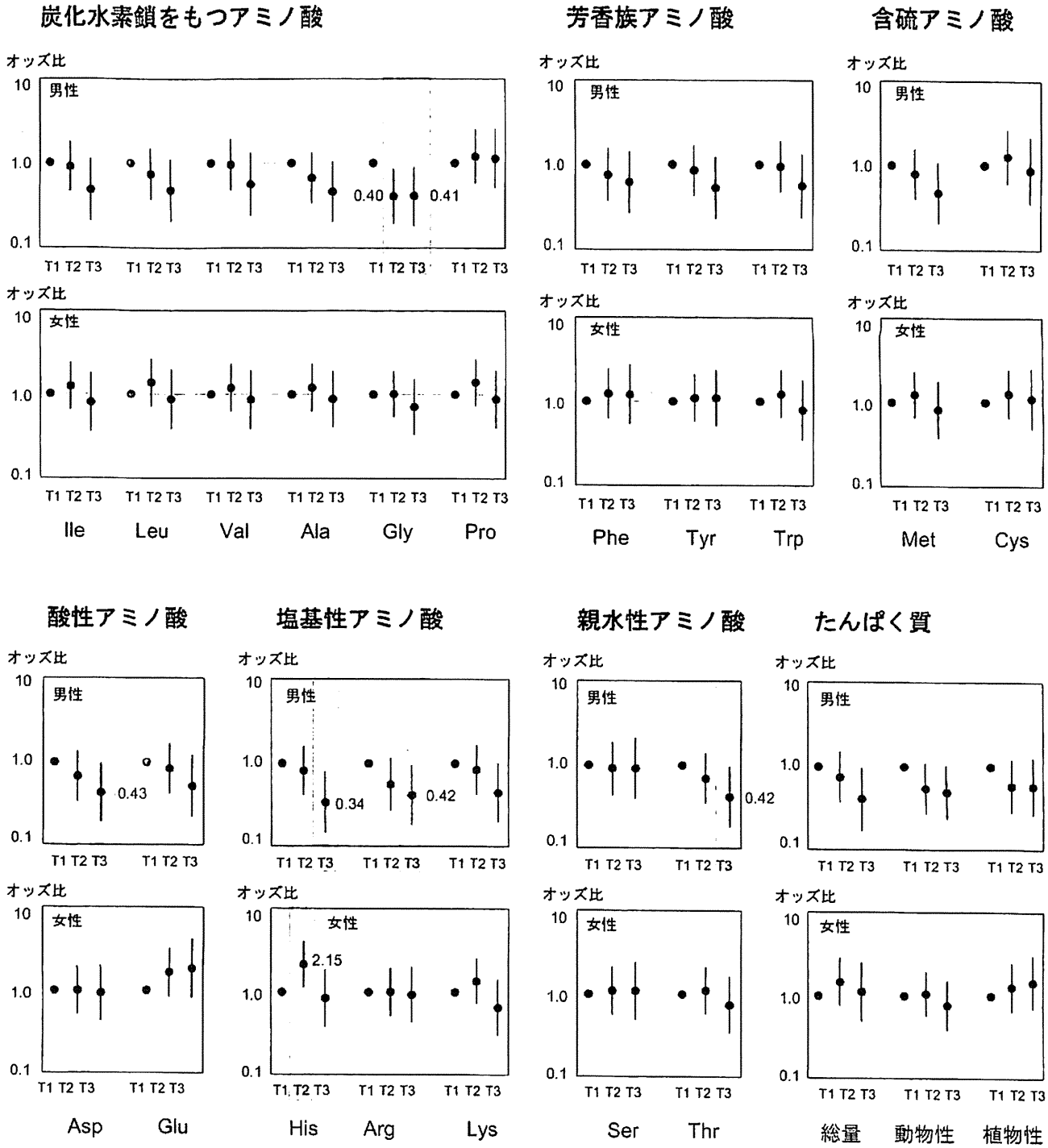

図1　18種のアミノ酸摂取量およびたんぱく質摂取量による抑うつのオッズ比
（男性：上段，女性：下段）

で有意差が認められた5種のアミノ酸の経口摂取量と抑うつとの関連についての報告はわれわれの知る限りない。

今後は抑うつとアミノ酸摂取量との関連を検証する研究が必須である。また各アミノ酸で抑うつに対する閾値が異なる可能性があり，抑うつに対するアミノ酸摂取量の量的関係についても検討していきたい。

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研究論文●32

地域在住中高年男性における定年退職後の就労と知能に関する縦断的検討

西田裕紀子　　丹下智香子　　森山　雅子　　富田真紀子
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日本未病システム学会

研究論文●32

地域在住中高年男性における定年退職後の就労と知能に関する縦断的検討

西田裕紀子[1)]　丹下智香子[1)]　森山　雅子[1,2)]　富田真紀子[1,2)]
安藤富士子[1,3)]　下方　浩史[1)]

1．背景と目的

定年退職は人生後半期の節目となる重大なライフイベントであり，定年退職後をどのように過ごすかは，個人の心身の状態に大きな影響を与える[1)]。特に，「定年退職後も働き続けるかどうか」ということは，知的な能力の保持などにも関連する重要な選択であると推測される。そこで本研究では，定年退職後の就労の有無が，定年退職の前後2年間における知能の変化に与える影響について，縦断的に検討する。なお，今回は，長期継続雇用を前提とする仕事に就く可能性が高く，定年退職を経験する割合の高い男性[2)]に焦点を当てることとする。

2．方法

1．対象

2年間隔で行われた「国立長寿医療研究センター・老化に関する長期縦断疫学研究(NILS-LSA)」の第2次調査(2000～2002)，第3次調査(2002～2004)，第4次調査(2004～2006)，第5次調査(2006～2008)，第6次調査(2008～2010)に少なくとも1回参加した中高年男性1,968名のうち，(a)第3次調査～第6次調査のいずれかで過去2年以内の定年退職経験を報告し，(b)その2年前の調査(定年退職前)にも参加していた，定年退職男性189名(平均年齢62.15±3.36歳)。NILS-LSAは，年齢および性により層化無作為抽出された地域住民を対象とした老化と老年病に関する縦断的コホート調査であり，独立行政法人国立長寿医療研究センター倫理委員会の了承の下に「調査への参加の文書による同意」の得られた者を対象として行われている[3)]。

2．変数

1）定年退職後の就労の有無

自記式の調査票により，定年退職後の就労の有無について回答を求め，定年退職後無職群と定年退職後有職群に分類した。

2）知能

定年退職前と定年退職後に行われた2回の個別面接において，ウェクスラー成人知能検査改訂版の簡易実施法(WAIS-R-SF)[4)]を施行し，①一般的事実や語彙などの知識量を測定する「知識」，②論理的範疇的思考力を測定する「類似」，③視覚的長期記憶の想起と照合の能力を測定する「絵画完成」，④情報処理の速さと正確さを測定する「符号」の得点(粗点)を求めた。

3）基本属性

自記式の調査票により，①過去2年以内の定年退職経験を報告した年齢，②教育年数，③定年退職前の調査時点における世帯年収(350万円未満，350万～549万円，550万～999万円，1000万円以上)に関する情報を収集した。

3．解析

1）定年退職後の就労の有無と基本属性との関連

定年退職経験を報告した年齢，教育年数については，

1）独立行政法人国立長寿医療研究センター予防開発部　2）名古屋大学大学院教育発達科学研究科　3）愛知淑徳大学健康医療科学部

表1 対象者の基本属性(定年退職後の就労の有無別)

	定年退職後無職群	定年退職後有職群	検定
定年退職経験(過去2年以内)を報告した年齢[a]	63.88±4.34	61.20±2.15	p<0.001[c]
教育年数[a]	12.53±2.88	12.78±3.16	n.s.[c]
定年退職前の世帯年収[b]			
350万円未満	6 (8.96)	4 (3.28)	
350万～549万円	15(22.39)	12(9.84)	p<0.05[d]
550万～999万円	26(38.81)	55(45.08)	
1000万円以上	19(28.36)	51(41.80)	

注1) [a]平均±S.D., [b]n(%)を示す。
注2) [c]t検定, [d]フィッシャーの正確確率検定による。
注3) 定年退職後無職群では、世帯年収を「わからない」と回答した者が1名いた。

定年退職後無職群，定年退職後有職群における差があるかどうかを検討するためにt検定を行った。一方，定年退職前の世帯年収については，定年退職後無職群，定年退職後有職群別に頻度を集計し，フィッシャーの正確確率検定を行った。

2) 定年退職後の就労の有無と知能の変化

目的変数として「知識」，「類似」，「絵画完成」，「符号」の各得点，説明変数として定年退職後の就労の有無(定年退職後無職群・定年退職後有職群)，調査時点(定年退職前・定年退職後)およびその交互作用項，調整変数として基本属性(定年退職経験を報告した年齢・教育年数・定年退職前の世帯年収)を投入した混合モデルを検討した。その際，被験者効果を変量効果として投入した。また，誤差共分散行列として一次の自己回帰を設定することで，定年退職前の測定値の影響を調整して解析を行った。

1)，2)ともに，解析にはSAS release 9.1.3を使用し，$p<0.05$を統計的有意とした。

3．結果

1．定年退職後の就労の有無と基本属性との関連

定年退職前の基本属性を定年退職後の就労の有無別に示す(表1)。定年退職経験を報告した年齢は，定年退職後有職群よりも定年退職後無職群の方が高かった。教育年数では定年退職後の就労による有意な差はみられなかった。一方，世帯年収では，定年退職後の就労により回答傾向に有意な偏りが認められ，定年退職後無職群では定年退職後有職群よりも「350万円未満」，「350～549万円」を選択する割合が高く，定年退職後有職群は定年退職後無職群よりも「550～999万円」，「1000万円以上」の選択率が高かった。

2．定年退職後の就労の有無と知能の変化

「知識」を目的変数とした混合モデルを検討した結果，定年退職後の就労と調査時点の主効果およびその交互作用はすべて有意ではなかった($F=0.34$, n.s.；$F=2.20$, n.s.；$F=0.74$, n.s.)。「類似」を目的変数とした場合にも，定年退職後の就労と調査時点の主効果およびその交互作用はすべて有意ではなかった($F=1.57$, n.s.；$F=0.25$, n.s.；$F=1.30$, n.s.)。同様に「絵画完成」を目的変数とした場合にも，定年退職後の就労と調査時点の主効果およびその交互作用は有意ではなかった($F=0.51$, n.s.；$F=2.63$, n.s.；$F=0.49$, n.s.)。一方，「符号」を目的変数にした場合，定年退職後の就労，調査時点の有意な主効果は認められなかったが($F=2.66$, n.s.；$F=0.68$, n.s.)，定年退職後の就労と調査時点の交互作用が有意であった($F=5.31$, $p<0.05$)。そこで定年退職後の就労別に調査時点の効果を検討した結果，定年退職後有職群では，定年退職前よりも定年退職後の「符号」得点が有意に高く($p<0.01$)，定年退職後無職群では，定年退職前と定年退職後の得点に有意な差は認められなかった(図1)。

4．考察

定年退職後の就労の有無は，定年退職した年齢や，定年退職前の世帯年収と関連することが示された。定年退

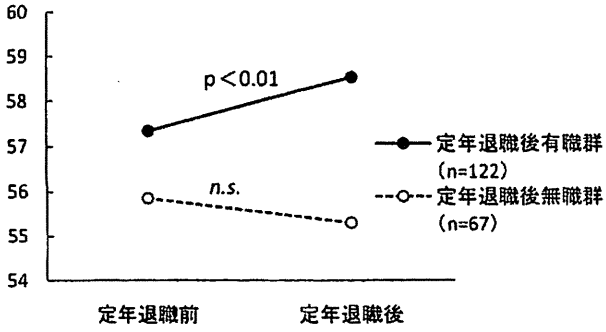

図1 定年退職前後の「符号」得点

注）定年退職後の就労の有無別に，定年退職を報告した年齢と教育年数，定年退職前の世帯年収を調整した最小二乗平均値を示す。

職後にも仕事を続ける男性は，定年退職時の年齢が比較的若く，定年退職前の世帯年収が高い傾向にあったことから，これらの基本属性は，定年退職後の就労継続を促す規定因になっていると考えられる。そのほかにも定年退職前の職種や，子どもの教育費や生活費に対する負担の大きさなど，多くの要因が定年退職をした後にも仕事をもつという選択に関連していると推測され，今後も検討が必要である。

さらに，定年退職後の就労が定年退職前後の変化に及ぼす影響は，知能の側面によって異なり，情報処理の速さと正確さを反映する「符号」の変化にのみ影響することが示された。これまでに，情報処理能力は加齢に伴って低下しやすい知能の側面であること[5]，情報処理能力の低下はほかの知能の側面の低下を引き起こす可能性があること[6]が指摘されており，中高年期において情報処理能力を保持するためには何が効果的なのかについて，関心が集まっている。定年退職後の高年齢者の雇用促進を目指す最近の社会状況[2]を考慮しても，本研究で得られた定年退職後に仕事をもつことが個人の情報処理能力の向上に役立つという結果は注目に値する。一方，知能の側面の中でも，一般的な知識力や論理的思考力，視覚的長期記憶の保持に対しては，就労以外の過ごし方が寄与する可能性がある。定年退職期の知能を向上させるための過ごし方を明らかにするためには，学習活動や社会活動，趣味などの幅広い生活スタイルを考慮に入れた，さらに長期的な検討を行う必要があるだろう。

付　記

本研究は，平成22年度科学研究費補助金萌芽研究「定年退職期の生活構造の変化と心理的健康に関する学際的縦断研究（課題番号19653072）」および平成22年度科学研究費補助金基盤研究(S)「中高年者のこころの健康についての学際的大規模縦断研究―予防へのストラテジーの展開（課題番号18109007）」により行われた。NILS-LSAにご参加いただいている愛知県大府市ならびに東浦町の住民の皆様に感謝いたします。

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研究論文● 6

自覚的健康度(SRH)が知能に及ぼす影響
—地域在住中高年者における8年間の縦断的検討—

安藤富士子　　西田裕紀子　　丹下智香子　　森山　雅子
富田真紀子　　下方　浩史

日本未病システム学会

研究論文●6

自覚的健康度(SRH)が知能に及ぼす影響
—地域在住中高年者における8年間の縦断的検討—

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富田真紀子[2)]　下方　浩史[2)]

1 緒言

自覚的健康度(SRH)は，高齢者のADL低下や死亡の予測因子として有用であることが報告されている[1,2)]。一方，加齢に伴う知能の低下や認知症の発症は高齢期のQOLの大きな阻害要因であり，その関連要因として食生活や運動習慣，知的活動や社会参加，喫煙や飲酒などの生活習慣や高血圧症，糖尿病，高脂血症などの生活習慣病などが挙げられている[3)]。SRHはこれら多数の要因を集約する要因として，加齢に伴う知能変化の単純かつ優れた予測因子となる可能性がある[4)]が縦断的な研究は限られている。

本研究では地域在住中高年者からの無作為抽出者を対象とした8年間の継続調査結果を用いてSRHが知能に及ぼす影響について検討した。

2 対象および方法

対象は「国立長寿医療研究センター・老化に関する長期縦断疫学研究(NILS-LSA)[5)]」参加者である。NILS-LSAは愛知県大府市ならびに知多郡東浦町在住の初回調査時40～79歳までの中高年者からの性・年代層化無作為抽出者で，調査への参加同意の得られた者を対象とした老化や老年病に関する縦断疫学研究であり，所属機関倫理委員会の承認を得て行われている。第1次調査は1997～2000年に行われ，以後2年ごとにほぼ同一の項目に関して追跡調査が行われている。

本研究ではNILS-LSAの第1次，第2次(2000～2002年)，第3次(2002～2004年)，第4次(2004～2006年)，第5次調査(2006～2008年)のすべてに参加した初回調査時40～79歳の男女1,205人(56.3±9.6歳，男性620人，女性585人)を対象とした。

SRHは第1次調査において自記式質問票を用いて「あなたの健康状態はいかがですか」という質問に対し5件法(大変よい，よい，普通，悪い，大変悪い)で回答を求めた。知能の指標としては第1次調査から第5次調査の各調査において，ウェクスラー成人知能検査改訂版簡易実施法(Wechsler Adult Intelligence Scale-Revised Short Form：WAIS-R-SF)[6)]を用いて4つの下位尺度(知識，類似，絵画完成，符号)得点を測定した。

統計解析には，SAS 9.1.3を用いた。対象を第1次調査のSRHによりSRH良好群(大変よい，よい)とSRH非良好群(普通，悪い，大変悪い)の2群に分類し，知能の各下位尺度得点(粗点)を目的変数，第1次調査時のSRHと調査時期(time)の主効果および交互作用を説明変数，性，年齢と一次自己回帰を調整変数とした混合モデルで，第1次調査時のSRHがその後の知能の推移に与える影響について検討した。すなわちモデル全体での主効果，交互作用の検討のほか，各調査時期のSRH 2群間の得点の比較および各SRH群内での調査時期間での得点比較(Tukeyの多重比較による)を行った。$p<0.05$を統計的有意とした。

1）愛知淑徳大学健康医療科学部　2）独立行政法人国立長寿医療研究センター予防開発部

表1　知能に対する自覚的健康度・調査時期の作用(主効果，交互作用のF値)

	知識	類似	絵画完成	符号
自覚的健康度(SRH)主効果	15.65****	7.74**	17.95****	10.54**
調査時期(time)主効果	22.44****	6.83****	31.50****	10.79****
SRH*time交互作用	0.92	2.87*	0.24	1.22

性，年齢，一次自己回帰を調整した混合モデルによる。*：p<0.05，**：p<0.01，****：p<0.0001

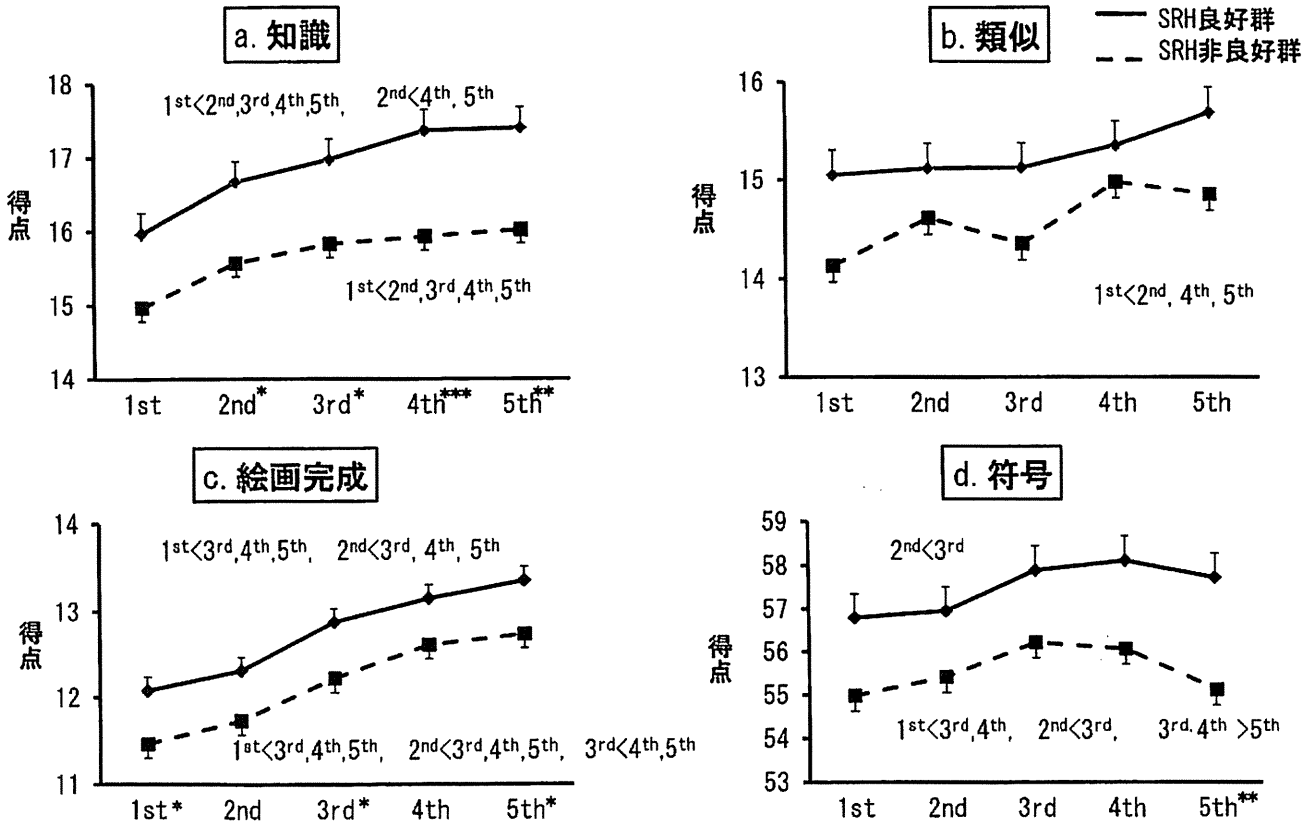

図1　自覚的健康度と知能(8年間の縦断変化)

NILS-LSAの第1次調査時の自覚的健康度(SRH)良好群(実線)と非良好群(点線)のWAIS-R-SF下位尺度(知識，類似，絵画完成，符号)の8年間の経時的変化を示した(性，年齢，一次自己回帰を調整した混合モデルによるlsmeans±S.E.)。1st：第1次調査，2nd：第2次調査，3rd：第3次調査，4th：第4次調査，5th：第5次調査。横軸のアスタリスク(*)は各調査時期における2群間の有意差を表している(*：p<0.05，**：p<0.01 ***：p<0.001)。グラフ中の不等号は各群内での調査時期間の多重比較(Tukey)の結果を表している。

3 結果

第1次調査時でのSRH良好群は357人(29.6%)，非良好群は848人(70.4%)であった。4つの下位尺度すべてで調査時期(time)とSRHの主効果を認め，SRH良好群では非良好群よりも得点が高かった(表1)。「知識」は，第1次調査ではSRHによる有意な得点差を認めなかったが，第2次調査以降SRH良好群で有意に得点が高く，得点差は経時的に開く傾向にあった(図1 a)。「類似」では調査時期とSRHの交互作用を認めた(表1)が，調査時期との一定の方向性をもった傾向は認められなかった(図1 b)。「絵画完成」ではSRH良好群，非良好群ともに経時的に得点が上昇する傾向を示した(図1 c)。「符号」では第5次調査においてSRH良好群の方が有意に得点が高かった。

また，SRH良好群では経時的に得点が低下しないのに対し，SRH非良好群では第3次，第4次調査に比べて第5次調査では得点が低下した(図1d)。

4 考察および結語

WAIS-R-SFの4つの下位尺度「知識」，「類似」，「絵画完成」，「符号」は，それぞれ「一般的な事実や事柄に関する知識量」，「論理的抽象的思考」，「視覚的長期記憶の想起と照合」，「情報処理のスピードと正確さ」を表すと考えられている[7]。今回の結果から，横断的にみると中高年者の知能，少なくともWAIS-R-SFで測定される知能の下位尺度に対してはSRHが有意に関連しており，SRHが高い者では知能得点が高いことが明らかとなった。また，第1次調査時のSRHの影響は8年後の知能得点にも影響を与えていた。SRHは特に「知能」と「符号」とに大きく影響を与え，SRHが優れない者では，知識を経時的に保持・増進する能力が低く，情報処理能力が早く衰えることが示唆された。

知識量を継続的に保つには，知識の繰り返しのインプットや積極的な知的活動が必要と考えられ，また，素早く的確に情報を処理するためには，集中力や運動機能も必要となる[8]。高齢者では痛みや疾患などで集中力が低下することが知られており，さらに身体的活動や知的活動の低下などSRH低下に関連している様々な要因が，縦断的な知能低下に関係している可能性があると考えられた。

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Synergistic interaction of cigarette smoking and alcohol drinking with serum carotenoid concentrations: findings from a middle-aged Japanese population

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Previous studies have indicated low serum carotenoid concentrations among cigarette smokers and/or alcohol drinkers, but little is known about the interaction of smoking and drinking with serum carotenoids. We tested the hypothesis that smoking and drinking reduce serum carotenoid concentrations synergistically. A total of 1073 subjects (357 male and 716 female) who had received health examinations in the town of Mikkabi, Shizuoka Prefecture, Japan, participated in the study. The subjects were divided into six groups according to alcohol intake (non-drinkers, <1 g/d; light drinkers, ≥ 1, <25 g/d; moderate-to-heavy drinkers, ≥ 25 g/d) and smoking status (non-smokers and current smokers). The dietary intakes and serum concentrations of six carotenoids (lycopene, α-carotene, β-carotene, lutein, β-cryptoxanthin and zeaxanthin) within each group were evaluated cross-sectionally. The dietary intakes of all carotenoids did not differ in the six groups after adjusting for age and sex. The multivariate-adjusted means of the serum carotenoid concentrations in non-drinkers did not differ between non-smokers and current smokers. In contrast, the adjusted means of serum α-carotene, β-carotene and β-cryptoxanthin were significantly lower than those with increased alcohol intake, and these lower serum carotenoids among alcohol drinkers were more evident in current smokers than in non-smokers. Serum lycopene of moderate-to-heavy drinkers was significantly lower than that of non-drinkers, but it was not influenced by smoking. Neither smoking nor drinking was associated with the serum concentrations of lutein and zeaxanthin. These results suggest that smoking and drinking may reduce the serum α-carotene, β-carotene and β-cryptoxanthin concentrations in a synergistic manner.

Carotenoids: Smoking: Alcohol drinking: Cross-sectional studies

Antioxidant micronutrients, such as vitamins and carotenoids, exist in abundance in fruit and vegetables and have been known to contribute to the body's defence against reactive oxygen species[1,2]. Numerous epidemiological studies have demonstrated that a high dietary consumption of fruit and vegetables rich in carotenoids or with high serum carotenoid concentrations results in lower risks of certain cancers, diabetes and CVD[3–8]. These epidemiological studies have suggested that antioxidant carotenoids may have a protective effect against these diseases.

On the other hand, active smokers are exposed to reactive free radicals that are present in cigarette smoke[9,10]. Therefore, smoking is a potent oxidative stress in humans[11–13]. Furthermore, alcohol drinking also induces reactive oxygen species during its metabolism in the liver[14–16]. Oxidants and free radicals induced by cigarette smoking and/or alcohol drinking can cause damage to lipids, proteins, DNA, carbohydrates and other biomolecules[17,18]. In such circumstances, antioxidant micronutrients, such as carotenoids, may play important roles in defending against oxidative stress by efficiently quenching the production of singlet oxygen and free radicals. Numerous epidemiological studies have shown that serum carotenoid concentrations were low among cigarette smokers and alcohol drinkers[19–31]. However, there is limited information about the synergistic interaction of cigarette smoking and alcohol drinking with serum carotenoid concentrations. The major serum carotenoids are lycopene, α-carotene, β-carotene, lutein, β-cryptoxanthin and zeaxanthin, and they account for more than 90 % of the circulating carotenoids in humans[32]. However, the differences in the change among these six major serum carotenoid concentrations against oxidative stress induced by cigarette smoking and alcohol drinking have not been thoroughly studied while controlling for dietary carotenoid concentrations.

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The present study aimed to investigate the interaction of cigarette smoking and alcohol drinking with the serum concentrations of the following main six carotenoid concentrations, i.e. lutein, lycopene, α-carotene, β-carotene, β-cryptoxanthin and zeaxanthin. The synergistic interaction of cigarette smoking and alcohol drinking with serum carotenoid concentrations was evaluated cross-sectionally.

Subjects and methods

Subjects

Data used in the present study were derived from health examinations of residents of the town of Mikkabi, Shizuoka Prefecture, Japan, aged from 30 to 70 years, in 2003 and 2005. Mikkabi is located in western Shizuoka, and about 40 % of its residents work in agriculture. In 2003, a total of 1979 males and females were subjects for the health examination. As a result, 1448 participants (73·2 % of the total) received a health examination. Informed consent was obtained from the 886 subjects (302 male and 584 female) recruited for the present study. The response rate was 61·2 %. In 2005, a total of 1891 males and females were subjects for the health examinations. As a result, 1369 participants (72·4 % of total subjects) underwent such an examination. Participants who had received the health examination in 2005 were further recruited for the present study, and informed consent was newly obtained from 187 subjects (fifty-five male and 132 female). As a result, a total of 1073 subjects were included in this survey.

In the present study, the following subjects were excluded from the data analysis: (1) those for whom the self-administered questionnaire data were incomplete; and (2) those for whom blood samples for serum carotenoid analysis were not collected. As a result, a total of 354 male and 715 female subjects were included for further data analysis.

Measurements

Blood samples were obtained in the morning after overnight fasting. Serum was separated from blood cells by centrifugation and stored at −80°C until analysis of the serum carotenoid concentrations. The concentrations of six serum carotenoids (lutein, lycopene, α-carotene, β-carotene, β-cryptoxanthin and zeaxanthin) were analysed by reverse-phase HPLC using β-apo-8′-carotenal as an internal standard at the laboratory of Public Health and Environmental Chemistry, Kyoto Biseibutsu Kenkyusho (Kyoto, Japan), as described previously[33]. The serum total cholesterol was measured using an autoanalyser using a commercial kit (Determiner TC-II C for serum total cholesterol; Kyowa-Medics, Inc., Tokyo, Japan) at the laboratory of the Seirei Preventive Health Care Centre (Shizuoka, Japan). Height and body weight were measured by trained public health nurses. BMI was calculated as the body weight (kg) divided by the height (m^2).

Lifestyle assessment and dietary data analysis

A self-administered questionnaire was used to collect lifestyle information, including tobacco use (current smoker, ex-smoker, or non-smoker), exercise (weekly participation), regular alcohol intake (one or more times per week) and dietary habits. The assessment of diet was a modification of the validated self-administered 121-item simple FFQ developed especially for the Japanese by Wakai and colleagues[34,35]. Information about alcohol consumption from Japanese *sake*, beer, *shochu*, wine and whisky, and the daily intake of eighteen nutrients from foods were estimated from monthly food intake frequencies with either standard portion size (for most types of food) or subject-specified usual portion size (for rice, bread, and alcoholic and non-alcoholic beverages) using the FFQ analysis software package for windows (Food Frequency Questionnaire System; System Supply Co., Ltd, Kanagawa, Japan). This FFQ analysis software computes an individual's food and nutrient intake from FFQ data on the basis of the Standard Tables of Food Composition in Japan[36]. The dietary carotenoid intakes of each individual were computed to obtain the amount of six carotenoids (lycopene, α-carotene, β-carotene, lutein, β-cryptoxanthin and zeaxanthin) using a published database of the carotenoid composition of fruit and vegetables[37,38]. In our survey, we calculated an individual's carotenoid intake from important sources of carotenoids. In this data analysis, the dietary carotenoid intakes were calculated from the FFQ data of each individual's food items, not dishes. The dietary intakes of six carotenoids and total energy intake of all subjects were used in the present report.

Statistical analysis

The dietary intakes and serum concentrations of carotenoids were skewed toward higher concentrations. These values were log (natural)-transformed to improve the normality of their distribution. The *t* test was used to compare the means of continuous variables in two groups. The χ^2 test was used to compare the rates of categorical variables in two groups. All variables were presented as an original scale. The data are expressed as the mean values and standard deviations, geometric mean values with 95 % CI, range, or percentages. In order to examine the relationship of independent variables with each serum carotenoid concentration, multiple regression analysis was performed with sex, age, BMI, smoking status, ethanol intake, serum total cholesterol, total energy intake excluding ethanol, and dietary intakes of respective carotenoids included always in the models as independent variables. The subjects were divided into three groups stratified by alcohol intake levels defined as non-drinker (< 1 g ethanol per d), light drinker (≥ 1 to < 25 g ethanol per d) and moderate and heavy drinkers (≥ 25 g ethanol per d) because one glass of Japanese *sake* (180 ml) or one bottle of beer (633 ml), which are major alcohol beverages and widely consumed in Japan, commonly contains about 25 g alcohol. In our study population, the number of ex-smokers was ninety-seven (9·1 % among the study population) from the self-administered questionnaire. However, in our survey, we did not collect data on time since last smoking. Therefore, ex-smokers were included in the non-smokers group. All subjects were categorised into six groups according to daily alcohol intake (non-drinkers, < 1 g/d; light drinkers, ≥ 1 to < 25 g/d; moderate-to-heavy drinkers, ≥ 25 g/d) and smoking status (current smokers and non-smokers, including ex-smokers). The multivariate adjusted mean of the dietary intakes and serum concentrations

of six carotenoids were calculated after adjusting for confounding factors. Differences in the multivariate adjusted mean of the dietary intakes and serum concentrations of six carotenoids among each group were tested by Bonferroni multiple comparison.

In our study population, the subjects who take carotenoid supplements were only 0·2 % among the study population. Therefore, we did not take account of carotenoid intake from supplements in the data analysis. The detection limit for the serum lycopene concentration for the method used in the study was 0·04 μg/ml (0·075 μmol/l), and values below the limit of detection of the assay were marked as 0·03 μg/ml (0·056 μmol/l) in the analysis. Each of the detection limits of other carotenoids was 0·02 μg/ml. In our survey, except for lycopene, there was no subject whose serum concentration of carotenoid was under the limit of detection. All statistical analyses were performed using the statistical software package SPSS for Windows (version 12.0J; SPSS Inc., Chicago, IL, USA) on a personal computer.

Ethical approval

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the ethics committee of the National Institute of Fruit Tree Science and the Hamamatsu University School of Medicine. Written informed consent was obtained from all subjects.

Results

Table 1 shows the characteristics of the study subjects stratified by sex. The dietary carotenoid intakes, excluding β-cryptoxanthin, were significantly higher in female than in male subjects. The serum carotenoid concentrations, excluding zeaxanthin, were significantly higher in female than in male subjects. The rates of current smokers and regular alcohol drinkers were higher in male than in female subjects.

Table 1. Characteristics of the study subjects

(Geometric means and 95 % confidence intervals, mean values and standard deviations or percentages)

	Male (*n* 354)		Female (*n* 715)	
	Geometric mean	95 % CI	Geometric mean	95 % CI
Age (years)				
Mean	56·3		54·6**	
SD	9·7		10·1	
BMI (kg/m^2)				
Mean	23·5		22·6***	
SD	2·9		3·1	
Total cholesterol (mmol/l)				
Mean	5·31		5·61***	
SD	0·86		0·90	
Total energy intake (kJ/d)				
Including ethanol				
Mean	9128·9		8370·0***	
SD	2277·4		2362·8	
Excluding ethanol				
Mean	8380·4		8319·1	
SD	2152·0		2364·8	
Ethanol intake (g/d)				
Mean	26·9		1·6***	
SD	31·2		4·9	
Dietary carotenoid intakes (mg/d)				
Lycopene	0·05	0·04, 0·06	0·07**	0·06, 0·08
α-Carotene	0·11	0·10, 0·12	0·24***	0·23, 0·26
β-Carotene	1·06	0·99, 1·13	1·70***	1·62, 1·77
Lutein	1·38	1·30, 1·47	1·92***	1·84, 2·00
β-Cryptoxanthin	0·30	0·25, 0·37	0·31	0·27, 0·37
Zeaxanthin	0·59	0·55, 0·65	0·70***	0·67, 0·75
Serum carotenoid concentrations (μmol/l)				
Lycopene	0·21	0·19, 0·23	0·31***	0·29, 0·33
α-Carotene	0·10	0·10, 0·11	0·15***	0·14, 0·16
β-Carotene	0·40	0·38, 0·43	0·74***	0·71, 0·77
Lutein	0·52	0·50, 0·55	0·57**	0·55, 0·58
β-Cryptoxanthin	1·03	0·93, 1·14	1·46***	1·37, 1·55
Zeaxanthin	0·22	0·22, 0·23	0·23	0·22, 0·23
Habitual exercise (%)‡	22·1		23·2	
Current smoker (%)	33·1		1·4†††	
Regular alcohol intake (%)‡	60·5		9·4†††	

Mean value was significantly different from that for the male subjects: ** $P<0·01$, *** $P<0·001$ (Student's *t* test).
††† Percentage was significantly different from that for the male subjects ($P<0·001$; χ^2 test).
‡ One or more times/week.

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Next, in order to examine the relationship of independent variables with each serum carotenoid concentration, multiple regression analysis was performed; sex, age, BMI, smoking status, ethanol intake, serum total cholesterol, total energy intake excluding ethanol, and dietary intakes of carotenoids were always included in the models as independent variables (Table 2). All six serum carotenoid concentrations were significantly associated with the dietary intakes of carotenoids. The strongest correlation between dietary intake and serum concentration was observed in β-cryptoxanthin. The serum total cholesterol was a significant positive predictor of the serum carotenoid concentration. The BMI was a significant negative predictor of serum carotenoid concentrations excluding β-cryptoxanthin. Smoking status was a significant negative predictor of the serum carotenoid concentration except for zeaxanthin. Ethanol intake was a significant negative predictor of the concentrations of serum lycopene, α-carotene, β-carotene and β-cryptoxanthin. Neither smoking status nor ethanol intake was associated with the serum zeaxanthin concentration.

Table 3 shows the results of the dietary carotenoid intakes in six groups stratified by daily alcohol intake and smoking status. The dietary intakes of α- and β-carotene in current smokers and/or in regular alcohol drinkers (>1 g/d) were significantly lower than those in non-smokers among non-drinkers. In addition, the dietary intake of lutein was significantly lower in moderate-to-heavy drinkers (more than 25 g/d) and in light drinkers (1–25 g/d) among current smokers than it was in non-smokers among non-drinkers. The dietary intake of β-cryptoxanthin was significantly lower in light drinkers (1–25 g/d) among current smokers than it was in non-smokers among non-drinkers. However, after adjusting for age and sex, these significantly lower dietary intakes of carotenoids were non-significant.

The unadjusted and adjusted means of the serum carotenoid concentration among the six groups are shown in Table 4. After adjusting for age and sex, the serum lutein and zeaxanthin concentrations were not different among the six groups stratified by daily alcohol intake and smoking status. In contrast, the serum lycopene concentration in moderate-to-heavy drinkers was significantly lower than that in non-drinkers. Although this lower serum lycopene concentration in moderate-to-heavy drinkers was observed in both non-smokers and current smokers, no significant difference was observed between non-smokers and current smokers. On the other hand, the concentrations of serum α-carotene, β-carotene and β-cryptoxanthin were significantly lower than those with increased alcohol intake. Furthermore, the serum α-carotene, β-carotene and β-cryptoxanthin of current smokers among regular alcohol drinkers (more than 1 g/d) were significantly lower than those of non-smokers who have the same alcohol intake. The lower serum carotenoid concentrations among regular alcohol drinkers were more evident in current smokers than in non-smokers. After further adjusting for BMI, total cholesterol, total energy intake excluding alcohol, and dietary intake of respective carotenoids, no obvious change in these associations of cigarette smoking and alcohol drinking with the serum carotenoid concentration was observed.

Furthermore, after multivariate adjusting, no obvious change of the present results about the differences in the

Table 2. Standard regression coefficients of each serum carotenoid concentrations with contributory factors*

	Lycopene		α-Carotene		β-Carotene		Lutein		β-Cryptoxanthin		Zeaxanthin	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Age	−0·329	<0·001	0·013	0·641	0·134	<0·001	0·128	<0·001	0·142	<0·001	0·015	0·619
Sex	0·024	0·523	0·017	0·655	0·121	<0·001	−0·032	0·435	−0·020	0·536	−0·081	0·044
BMI	−0·098	<0·001	−0·126	<0·001	−0·165	<0·001	−0·133	<0·001	−0·031	0·179	−0·093	0·001
Smoking status	−0·074	0·033	−0·182	<0·001	−0·177	<0·001	−0·118	0·002	−0·146	<0·001	−0·067	0·071
Ethanol intake	−0·167	<0·001	−0·167	<0·001	−0·240	<0·001	0·047	0·175	−0·174	<0·001	0·014	0·675
Total cholesterol	0·262	<0·001	0·205	<0·001	0·212	<0·001	0·277	<0·001	0·146	<0·001	0·315	<0·001
Total energy intake excluding ethanol	−0·034	0·216	−0·074	0·007	−0·103	<0·001	−0·033	0·312	−0·069	0·003	−0·039	0·220
Dietary intake of corresponding carotenoid	0·170	<0·001	0·224	<0·001	0·171	<0·001	0·119	<0·001	0·492	<0·001	0·239	<0·001
R^2 adjusted	0·249		0·264		0·409		0·140		0·455		0·145	

*Standard regression coefficients of each serum carotenoid concentrations with independent variables were calculated by multiple linear regression analysis included always in the models as independent variables.

Table 3. Unadjusted and adjusted dietary carotenoid intakes stratified by smoking status and daily alcohol intake

(Geometric means and 95 % confidence intervals, mean values and standard deviations or percentages)

	Daily alcohol intake											
	< 1 g/d				≥ 1 to < 25 g/d				≥ 25 g/d			
	Non-smokers (*n* 579)		Current-smokers (*n* 29)		Non-smokers (*n* 263)		Current-smokers (*n* 35)		Non-smokers (*n* 100)		Current-smokers (*n* 63)	
	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI
Age (years)												
Mean	55·8		53·4		53·8		49·3**		57·1		55·6	
SD	9·9		10·0		10·2		9·3		9·6		9·9	
Male (%)	7·8		82·8		37·6		88·6		93·0		98·4	
BMI (kg/m^2)												
Mean	22·8		22·9		22·8		23·1		23·7		22·7	
SD	3·2		3·5		2·8		2·7		2·9		2·6	
Serum total cholesterol (mmol/l)												
Mean	5·60		5·49		5·49		5·35		5·35		5·20*	
SD	0·88		0·91		0·90		0·82		0·89		1·06	
Total energy intake (kJ/d)												
Including ethanol												
Mean	8379·8		8366·0		8512·5		8856·7		9433·8***		9992·0***	
SD	2462·5		1622·6		2102·2		2197·4		2174·1		2408·1	
Excluding ethanol												
Mean	8377·5		8361·7		8301·3		8527·3		8091·5		8426·5	
SD	2462·5		1621·3		2092·7		2186·4		2059·8		2239·7	
Ethanol intake (g/d)												
Mean	0·1		0·1		6·4***		10·6***		49·6***		57·3***	
SD	0·2		0·2		5·9		7·2		24·6		35·9	
Dietary carotenoid intakes (mg/d)												
Lycopene												
Crude	0·07	0·06, 0·08	0·05	0·02, 0·12	0·07	0·05, 0·08	0·04	0·02, 0·08	0·06	0·04, 0·08	0·04	0·03, 0·07
Adjusted†	0·06	0·05, 0·07	0·06	0·03, 0·13	0·07	0·05, 0·09	0·05	0·02, 0·09	0·07	0·04, 0·10	0·05	0·03, 0·09
α-Carotene												
Crude	0·23	0·21, 0·24	0·14*	0·10, 0·19	0·18**	0·16, 0·20	0·14*	0·10, 0·20	0·12***	0·10, 0·14	0·09***	0·07, 0·12
Adjusted†	0·19	0·18, 0·21	0·20	0·15, 0·27	0·19	0·17, 0·21	0·21	0·16, 0·28	0·18	0·15, 0·22	0·15	0·12, 0·18
β-Carotene												
Crude	1·68	1·60, 1·76	1·17**	0·89, 1·53	1·37***	1·26, 1·48	1·04***	0·80, 1·36	1·10***	0·98, 1·23	0·99***	0·83, 1·17
Adjusted†	1·49	1·40, 1·58	1·49	1·18, 1·87	1·42	1·31, 1·52	1·42	1·14, 1·75	1·41	1·23, 1·61	1·32	1·11, 1·56
Lutein												
Crude	1·89	1·80, 1·99	1·51	1·19, 1·92	1·68	1·56, 1·80	1·34*	1·06, 1·70	1·37***	1·23, 1·54	1·40**	1·20, 1·65
Adjusted†	1·74	1·64, 1·83	1·79	1·43, 2·23	1·72	1·60, 1·85	1·66	1·35, 2·04	1·65	1·44, 1·88	1·73	1·47, 2·03
β-Cryptoxanthin												
Crude	0·39	0·33, 0·46	0·16	0·07, 0·41	0·25	0·19, 0·33	0·10**	0·04, 0·25	0·30	0·20, 0·45	0·25	0·16, 0·41
Adjusted†	0·38	0·32, 0·45	0·18	0·09, 0·36	0·28	0·22, 0·36	0·16	0·08, 0·30	0·23	0·15, 0·35	0·22	0·13, 0·37
Zeaxanthin												
Crude	0·69	0·64, 0·74	0·55	0·40, 0·75	0·68	0·62, 0·75	0·62	0·48, 0·80	0·57	0·49, 0·66	0·65	0·52, 0·80
Adjusted†	0·66	0·61, 0·71	0·59	0·44, 0·80	0·68	0·62, 0·75	0·67	0·50, 0·88	0·63	0·53, 0·75	0·72	0·58, 0·89

Mean value was significantly different from that of non-smoking non-drinkers: * $P<0·05$, ** $P<0·01$, *** $P<0·001$ (Bonferroni multiple comparison test).

† Age and sex were adjusted.

Table 4. Unadjusted and adjusted serum carotenoid concentrations stratified by smoking status and daily alcohol intake
(Geometric means and 95 % confidence intervals)

	Daily alcohol intake											
	< 1 g/d				≥ 1 to < 25 g/d				≥ 25 g/d			
	Non-smokers		Current-smokers		Non-smokers		Current-smokers		Non-smokers		Current-smokers	
Serum carotenoids (μmol/l)	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI	Geometric mean	95 % CI
Lycopene												
Crude	0·30	0·29, 0·32	0·24	0·19, 0·31	0·29	0·27, 0·32	0·21	0·17, 0·28	0·19***	0·16, 0·22	0·17***	0·14, 0·20
Adjusted§	0·29	0·28, 0·31	0·26	0·20, 0·33	0·28	0·26, 0·31	0·21	0·17, 0·26	0·21**	0·18, 0·25	0·19***	0·15, 0·22
Adjusted‖	0·30	0·28, 0·32	0·24	0·19, 0·31	0·28	0·26, 0·30	0·20*	0·16, 0·25	0·21***	0·18, 0·24	0·19***	0·16, 0·22
α-Carotene												
Crude	0·14	0·14, 0·15	0·10**	0·09, 0·12	0·13	0·13, 0·14	0·09***†††	0·08, 0·11	0·09***	0·09, 0·10	0·07***†††‡	0·06, 0·08
Adjusted§	0·14	0·13, 0·14	0·11	0·10, 0·14	0·14	0·13, 0·14	0·10*†	0·09, 0·12	0·11**	0·10, 0·12	0·08***††	0·07, 0·09
Adjusted‖	0·14	0·13, 0·14	0·11	0·09, 0·13	0·13	0·13, 0·14	0·10**††	0·09, 0·12	0·11***	0·10, 0·12	0·08***††	0·07, 0·09
β-Carotene												
Crude	0·74	0·71, 0·77	0·50**	0·41, 0·60	0·63**	0·59, 0·67	0·35***†††	0·28, 0·45	0·38***	0·34, 0·42	0·25***††††‡‡	0·22, 0·29
Adjusted§	0·66	0·63, 0·70	0·61	0·51, 0·74	0·65	0·61, 0·70	0·47**†	0·40, 0·57	0·46***	0·41, 0·52	0·32***††‡‡	0·28, 0·37
Adjusted‖	0·67	0·64, 0·70	0·58	0·49, 0·70	0·65	0·61, 0·69	0·46***††	0·39, 0·54	0·46***	0·41, 0·51	0·32***††‡‡	0·28, 0·36
Lutein												
Crude	0·60	0·58, 0·62	0·52	0·45, 0·61	0·59	0·57, 0·62	0·47**††	0·40, 0·54	0·59	0·55, 0·64	0·55	0·50, 0·61
Adjusted§	0·58	0·56, 0·60	0·56	0·49, 0·64	0·60	0·58, 0·63	0·52	0·45, 0·59	0·62	0·57, 0·67	0·59	0·53, 0·66
Adjusted‖	0·58	0·56, 0·60	0·54	0·47, 0·62	0·60	0·57, 0·63	0·51	0·45, 0·57	0·62	0·57, 0·67	0·59	0·53, 0·65
β-Cryptoxanthin												
Crude	1·55	1·45, 1·65	1·01	0·71, 1·44	1·34	1·21, 1·48	0·62***†††	0·44, 0·86	0·98***	0·82, 1·17	0·61***††	0·49, 0·76
Adjusted§	1·49	1·38, 1·60	1·11	0·83, 1·48	1·41	1·28, 1·55	0·78***†††	0·60, 1·02	0·95***	0·80, 1·13	0·62***††‡	0·50, 0·77
Adjusted‖	1·44	1·35, 1·53	1·20	0·94, 1·54	1·43	1·32, 1·55	0·87**†††	0·70, 1·10	1·00***	0·87, 1·16	0·67***†††‡	0·56, 0·80
Zeaxanthin												
Crude	0·24	0·24, 0·25	0·23	0·21, 0·27	0·25	0·24, 0·26	0·22	0·20, 0·24	0·24	0·23, 0·26	0·24	0·22, 0·26
Adjusted§	0·24	0·23, 0·25	0·24	0·21, 0·27	0·25	0·24, 0·26	0·23	0·20, 0·25	0·24	0·23, 0·26	0·24	0·22, 0·26
Adjusted‖	0·24	0·23, 0·25	0·24	0·21, 0·26	0·25	0·24, 0·25	0·22	0·20, 0·25	0·24	0·23, 0·26	0·24	0·22, 0·26

Mean value was significantly different from that of non-smoking non-drinkers: * $P<0·05$, ** $P<0·01$, *** $P<0·001$ (Bonferroni multiple comparison test).
Mean value was significantly different from that of non-smokers who have the same alcohol intake: † $P<0·05$, †† $P<0·01$, ††† $P<0·001$ (Bonferroni multiple comparison test).
Mean value was significantly different from that of non-drinking current smokers: ‡ $P<0·05$, ‡‡ $P<0·01$, ‡‡‡ $P<0·001$ (Bonferroni multiple comparison test).
§ Age and sex were adjusted.
‖ Age, sex, BMI, total cholesterol, total energy intake excluding alcohol, and dietary intake of corresponding carotenoid were adjusted.

changes among the serum concentrations of six carotenoids stratified by cigarette smoking and alcohol drinking habits were observed, even though female subjects were excluded (data not shown).

Discussion

The original FFQ we used in the present survey is not able to estimate the amount of carotenoid intake from foods because all six carotenoid contents in each food are not assessed in standard tables of food composition in Japan. However, recently, a database of the carotenoid composition of fruit and vegetables was published[37,38]. In the present study, we adapted FFQ analysis software package to calculate an individual's carotenoid intake from important sources of carotenoids, and significant relationships between dietary intake of each carotenoid and its serum levels were observed. This is the first experiment to estimate six dietary carotenoids in Japan.

The present investigation is the first-reported cross-sectional study to examine the synergistic interaction of cigarette smoking and alcohol drinking with the six major serum carotenoids while controlling for dietary carotenoid intakes. The results indicated that daily alcohol intake may reduce the serum concentrations of lycopene, α-carotene, β-carotene and β-cryptoxanthin in a dose-dependent manner. Furthermore, these alcohol-related lower serum carotenoid concentrations, except for lycopene, were more evident in current smokers than in non-smokers. The serum lycopene concentration seems to be influenced by alcohol drinking and not by smoking. In addition, neither smoking nor alcohol drinking affected the serum lutein and zeaxanthin concentrations.

Although many epidemiological studies have indicated that the serum carotenoid concentrations were low among current smokers and/or regular alcohol drinkers[19–31], most of these previous studies evaluated the effect of these lifestyle factors on the serum carotenoid concentrations separately. It is widely known that the dietary intake of carotenoids is lower in smokers than in non-smokers, in alcohol drinkers than in non-drinkers, and in males than in females[21]. In addition, the consumption of alcohol among smokers is higher than that among non-smokers. Therefore, the possibility that the correlation between cigarette smoking and alcohol drinking with the serum carotenoid concentrations observed in these previous reports would be an artifact of the strong correlation of cigarette smoking and alcohol drinking could not be ruled out. In our data analysis, the subjects were stratified into six groups according to their smoking status and the amount of daily alcohol intake. Thus, we believe that the influence of the association among cigarette smoking and alcohol drinking can be completely eliminated in the analysis of these six subgroups.

Previously, seven cross-sectional studies have reported the possibility that cigarette smoking and alcohol drinking might synergistically enhance the depletion of serum carotenoid concentrations[19–23,25,26]. However, these studies did not take into account the dietary intakes of carotenoids; therefore, it is not clear whether the low serum carotenoid concentration was due to the low dietary intake of carotenoids or whether cigarette smoking and alcohol drinking would cause deterioration in the serum carotenoid concentrations. To our knowledge, there have been no reports about the synergistic interaction of cigarette smoking and alcohol drinking with the serum carotenoid concentrations after taking into account the dietary carotenoid intakes. Furthermore, there is limited information about the differences in the changes among the serum concentrations of the six major carotenoids against oxidative stress induced by cigarette smoking and alcohol drinking. In our data analysis, the dietary intakes of α-carotene, β-carotene and lutein in current smokers and/or regular alcohol drinkers were significantly lower than those in non-smokers among non-drinkers. However, these significantly lower dietary intakes became insignificant after adjusting for age and sex. Furthermore, a significant synergistic interaction of cigarette smoking and alcohol drinking with the serum carotenoid concentrations was observed after further adjusting for the dietary intakes of respective carotenoids. Therefore, it seems that the significant differences of the multivariate adjusted means of the serum carotenoid concentrations among the six groups stratified by lifestyle factors might be caused by the depletion of serum carotenoids and not by differences in dietary carotenoid intakes.

Recently, some animal experiments have been reported concerning the synergistic effect of cigarette and alcohol on the antioxidant defence system in several tissues[39–41]. These animal experiments show the possibility that combination of alcohol plus cigarette smoke induces the excessive generation of reactive oxygen species and free radicals to a greater extent than that from alcohol or cigarette smoke alone. Thus, the combination of cigarette smoking and alcohol drinking might induce the excessive generation of free radicals and cause the marked depletion of serum carotenoid concentrations of regular alcohol drinkers among current smokers than those of non-smokers who have the same alcohol intake.

It is also known that a transforming reaction from pro-vitamin A to retinol is induced by smoking[42]. On the other hand, alcohol is known to promote increased oxidation of vitamin A compounds and reduced liver stores[43]. It can be postulated that alcohol intake may also accelerate the conversion of pro-vitamin A to retinol[44]. From among the six major serum carotenoids we measured, α-carotene, β-carotene and β-cryptoxanthin are pro-vitamin A. These three carotenoids are converted to retinol in the body. Therefore, the serum concentrations of α-carotene, β-carotene and β-cryptoxanthin might be more easily influenced by cigarette smoking and alcohol drinking than lycopene.

In the present study, serum lutein and zeaxanthin concentrations were not influenced not only by alcohol drinking but also by cigarette smoking. We have no clear explanation for these inconsistencies with previous results[25,27–29,31]. We concluded that lutein and zeaxanthin might be difficult to be exposed to oxidative stress or that the differences among the six serum carotenoids observed occurred by chance. One possible explanation is that the differences in the associations of the six serum carotenoids with cigarette smoking and alcohol drinking might be attributed to the polar characteristics of each carotenoid. It is conceivable that the tissue distribution and localisation in the cell membranes of carotenoids differ in each carotenoid. Especially, the chemical structure of a carotenoid may determine its localisation in a cell membrane. Hydrocarbon carotenoids, such as lycopene, α-carotene and

β-carotene, are located within the hydrophobic membrane core with multiple orientations, whereas xanthophylls, such as lutein and zeaxanthin, have a more rigid membrane-spanning orientation[45]. Therefore, we believe that the antioxidant defence system by carotenoids against lipid peroxidation in a cell membrane depends on the polar characteristics of each carotenoid. Alternatively, as another one possible explanation for the differences in the associations of the six serum carotenoids with cigarette smoking and alcohol drinking, we consider the differences of carotenoid distribution in lipoproteins. Lipid-soluble carotenoids are carried by lipoproteins from the liver into the blood circulation. Hydrocarbon carotenoids, such as lycopene, α-carotene and β-carotene, are mainly found in LDL, whereas xanthophylls are equally found in HDL and LDL[46]. Recent studies indicate that oxidised LDL increases in smokers and/or heavy alcohol drinkers[47,48]. Therefore, it is conceivable that the plasma clearance rate of carotenoids might be influenced by oxidised LDL induced by cigarette smoking and alcohol drinking.

The present study had some limitations. First, we could not evaluate the association of blood concentrations of vitamins C and E with cigarette smoking and alcohol drinking. It would be necessary to measure the blood concentrations of vitamins C and E in order to examine the associations of these antioxidant vitamin concentrations with these lifestyle factors. Second, the data obtained here consisted of cross-sectional analyses. Therefore, only limited inferences can be made regarding temporality and causation. Third, in the present study, the sample size of current smokers was not particularly large. Therefore, it was impossible to examine the quantitative effects of cigarette smoking on the serum carotenoid concentration. Further studies on a large scale will be required. Fourth, seasonal influence was not considered in the present study, but it could be important to consider this influence in future studies. Last, our findings might be specific to middle-aged Japanese. Further studies in other races and/or regions will be required.

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M. S. was responsible for study design, data collection, and data management and carried out the data analysis and wrote the manuscript. M. N. was responsible for study design, data collection, and data management and assisted in manuscript preparation. K. O., Y. I., H. M., F. A., H. S. and M. Y. were involved in the data collection and assisted in manuscript preparation. All the authors provided suggestions during the preparation of the manuscript and approved the final version submitted for publication.

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特集

健康食品をめぐって

サプリメントの有効性の疫学研究

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