

Investigations on taste blindness with thiocarbamides

II (1). Intra-pair discrepancy of taste in pairs of identical twins

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Ardashnikov, Lichtenstein, Martynova, Soboleva, and Postnikova (2) were the first to report that in pairs of twins which on the basis of the customary and carefully performed polysymptomatological examination, *i.e.* by analysis of « external similarity », have to be considered identical twins intra-pair discrepancy in ability to taste *phenylthiocarbamide* (PTC) may occur. On 137 pairs of identical twins there were found to be 3 of which one of the members found the said compound bitter, whereas the other member considered it tasteless. Unfortunately no statement was made about the way in which the test in question was performed.

A couple of years later Rife (3) found 3 such cases on 31 pairs of twins which with great care had been classed as identical twins as indicated above. Here again the way in which the test was performed unfortunately was not stated.

During the World Twin Congress held at Eindhoven (Netherlands) in July 1957 we tested 70 pairs of twins, which on the basis of a polysymptomatological examination performed under the direction of Dr. J. W. Bruins (Deventer) had to be considered identical twins, for their ability to taste *para-ethoxyphenylthiocarbamide* (EPTC). The way in which the test was carried out was the same as in our earlier work on taste blindness (1): 10 ml of a solution 1:5,000 (200 mg per litre) of EPTC in distilled water, warmed to about 37°, was supplied, *i.e.* a quantity amply sufficient to bring all the taste buds almost immediately into contact with the solution.

The two members of 23 pairs of twins thought the solution tasteless, those of 44 pairs found it bitter. The two members of 1 pair considered the solution very faintly sweet. We do not attach much value to the latter fact, since the two test persons in question were not very positive in their judgment and no further test could be performed. However, the question may be raised whether such « abnormal » judgments about the taste of EPTC (and other appropriate thiocarbamides) — which have been repeatedly reported (4) and thus may undoubtedly be real — are hereditary.

In 2 of the pairs of identical twins tested by us a clear intra-pair discrepancy of

taste was encountered; one of the members found the solution in question distinctly bitter, whereas the other member considered it completely tasteless.

The phenomenon observed by Ardashnikov *c. s.* (2) and by Rife (3) for PTC therefore occurs with EPTC as well.

It is known that within single individuals considerable variations in taste sensitivity for thiocarbamides, *i. e.* considerable variations in taste threshold concentration, can occur. Typical cases of this remarkable fact were first found by Salmon and Blakeslee (5), and led these investigators to the statement that « the taste world of any one individual is not a stable one »; we here only recall the most striking case mentioned by the said investigators: on three occasions a subject could detect a bitter taste in a solution 1:2,560,000 of PTC, but once she was not able to detect this taste until the solution was 256 times so strong, namely was of the concentration 1:10,000. Verkade, van Hulssen, and Wepster (1) found that of 440 test persons who detected a bitter taste in a solution 1:80,000 of EPTC, a few weeks later 16 found a solution 1:5,000 of said compound tasteless. If these 16 test persons had been tested only with the aid of the latter solution at the moment in question, they would have been wrongly classified as non-tasters, because the investigators mentioned had adopted somewhat arbitrarily, but surely by no means unreasonably, the concentration 1:5,000 as « taste blindness threshold concentration ».

As already observed elsewhere (1), these often considerable individual variations in taste threshold concentration, which may occur within a very short time, have quite wrongly received no attention in the work on the heredity of taste blindness hitherto performed. At least, to our knowledge the contrary is not apparent from the literature. It is evident that in work of this nature a single test with a solution of the adopted « taste blindness threshold concentration » — we leave out of account the use of crystals of the thiocarbamide employed or of paper impregnated with it, since this practice, as explained elsewhere (1), is quite objectionable — will never be sufficient. Notwithstanding this, it must be stated that until now it has been rather common to perform tests with only one solution.

It appeared quite possible to us *a priori* that the intra-pair discrepancy in ability to taste a given thiocarbamide encountered in identical twins might be due to an incidental and temporary rise of the taste threshold concentration in one of the members of the pair above the adopted « taste blindness threshold concentration ». In order to gain certainty about this, we gave the two pairs of identical twins found by us to exhibit the intra-pair discrepancy in question (M.P. and E.P., ♀, 25 years of age, and W.V. and G.V., ♀, 19 years of age) the solution 1:5,000 of EPTC to taste every week for about six months. The result was invariably the same: one member of each pair (E.P. and G.V.) always found the solution distinctly bitter, whereas the other member (M.P. and W.V.) always considered it completely tasteless. From this it may in our opinion be positively concluded that the intra-pair discrepancy in ability to taste EPTC (or other thiocarbamides) found in these pairs of identical twins will have to be accounted for in some other way.

It also appeared desirable to us to have at least some notion of the difference in taste threshold concentration between the two members of each of our pairs of identical twins. For this purpose we gave them to taste, besides the solution 1:5,000 adopted by us as « taste blindness threshold », solutions 1:10,000, 1:20,000, 1:40,000, 1:80,000, 1:160,000, and 1:320,000 of EPTC. The results of these tests were as follows:

W. V. found all solutions tasteless. For G. V. on the contrary the solution 1:5,000 was very strongly bitter and the bitterness distinctly decreased as the dilution of the solution increased, until with the solution 1:320,000 only a faintly bitter taste was perceived. In this case therefore the intra-pair discrepancy was particularly striking.

In the other pair the intra-pair discrepancy was less pronounced, but still it was unmistakably present. M.P. found all solutions tasteless. To E.P. on the contrary all solutions were (faintly) bitter, though it was not possible to ascertain a distinct correlation between the concentration of the solution and the emotional response to its taste. Blakeslee (6) was the first to point out the occasional absence of this correlation; he mentioned, among others, a perfectly analogous example.

Finally it is to be noted that the case of the test persons W. V. and M. P. was decidedly not one of a general taste deficiency; we carefully convinced ourselves of this. In this connection it may be mentioned in passing that in a case, found by Rife (7), of intra-pair discrepancy in ability to taste PTC in a pair of identical twins the « non-taster » was later shown to have a general taste deficiency, which was possibly due to a severe poliomyelitis several years previously. In the introduction of the present paper this case has naturally been left out of consideration.

Numerous investigations, of which we here cite only a few (6, 8-13), have positively led to the result that taste blindness is hereditary. As far as we are aware, it is generally accepted that the two types of individuals, « tasters » and « non-tasters », differ in respect of a single pair of genes, the « tasters » being homozygous or heterozygous for the dominant allele, the « non-tasters » homozygous for the recessive allele. This implies of course that the two members of a pair of identical twins in principle have to behave similarly towards thiocarbamides; in actual fact v. Skramlik (14) found strikingly similar taste threshold concentrations for three thiocarbamides in such a pair of twins. Discrepant behaviour such as was positively established, as appears from the above, by ourselves and by others, must then have an exogenic cause, the nature of which is obviously unknown; in this connection Ardashnikov *c. s.* (2) speak of a « phenotype variation of the gene for PTC », but it would seem to us that this expression is not very well-chosen. In the « non-tasters » of the pairs of identical twins in question the taste threshold concentration has been raised by an exogenic cause about which we know nothing and has come to lie above the (somewhat arbitrarily adopted) « taste blindness threshold concentration » — 1:5,000 for PTC and EPTC. These members of the pairs have thus become *crypto tasters*. We shall discuss this view somewhat more fully below.

For a better understanding of the above we would recall that the fairly common term « taste blindness » has unfortunately been a bad choice. In fact, we do not have

to do with an absolute taste deficiency for the thiocarbamide under consideration, but with a consequence of the remarkable form of the taste threshold concentration frequency curve. This curve is bimodal; one frequency maximum lies at a very low, the other at a relatively high concentration. According to Blakeslee (6) « all persons can taste bitterness in the compound if only it can be gotten to the taste organs in a sufficiently concentrated condition ». While for most persons, the « tasters », very low concentrations suffice, another and also numerous group of persons, the « non-tasters », require the use of much higher concentrations. An intermediate concentration range is quantitatively of little importance with regard to the taste threshold; in this range the « taste blindness threshold concentration » is chosen somewhat arbitrarily. This view, which is due to Blakeslee (6), was completely confirmed by later investigations of Hartmann (15), Falconer (16), Harris and Kalmus (17), and others; we refer particularly to Hartmann's paper, which contains a few illustrative graphs.

Hartmann (18) already pointed out that the bimodality of the taste threshold concentration/frequency curve implies the existence of « tasters » and « non-tasters » in whom the taste threshold concentration lies on the « wrong » side of the chosen « taste blindness threshold concentration » and who consequently are classified as non-tasters and tasters respectively, but actually wrongly so. Such persons are what we would like to call « *crypto tasters* » and « *crypto non-tasters* ». The existence of the former category now finds a confirmation in the discrepant behaviour of the members of certain pairs of identical twins.

Unfortunately it is not possible to obtain solutions of EPTC the concentration of which lies above the chosen « taste blindness threshold concentration » (1:5,000) to an extent that is of real value with a view to the present work. We gave both subjects in question (M. P. and W. V.) a solution 1:2,000 of EPTC to taste. One of them (W. V.) considered this solution faintly bitter; in her case the taste threshold concentration was thus actually found to lie on the « wrong » side of the « taste blindness threshold concentration ».

It may be added here that a few tests were performed on the parents of each of our two pairs of twins; they reacted differently to EPTC, one being a « taster » and the other a « non-taster ». Most probably — this restriction is a consequence of the work described in the present paper — both pairs of twins under consideration were therefore heterozygous.

It must not remain unmentioned here that Gottschick (19) thinks the discrepant behaviour towards thiocarbamides of the two members of the pairs of twins discussed above has to be interpreted in an altogether different and curious way. In fact, according to this investigator the conclusion that must be drawn from this discrepant behaviour is that the respective pairs of twins were positively not uniovular. His criticism is directed in particular against the polysymptomatological examination introduced by Siemens, Verschuer, and others, *i.e.* against the ascertainment of the identity of pairs of twins on the basis of especially external similarity. This may appear from the following quotation (in which EZ stands for identical twins and ZZ for fraternal

twins): « Das Aehnlichkeitsverfahren ... beruht auf der nicht ganz zutreffenden Annahme, dass sich EZ einerseits nie so unähnlich sehen wie ZZ, und ZZ andererseits nie so ähnlich wie EZ. Wieweit das aber wirklich zutrifft, ist meines Wissens bisher überhaupt noch nie empirisch nachgeprüft worden. Vor allen Dingen muss bedacht werden, dass die Mehrzahl der zur Eiigkeitsdiagnose herangezogenen « Erbmerkmale » sehr stark von Umweltsunterschieden mit beeinflusst wird, und zwar sicher in stärkerem Masse, als das, die Eiigkeitsdiagnosen der 148 EZ als richtig hingenommen, bei den Geschmacksdifferenzen des PTC der Fall sein würde. Diese Umweltsunterschiede können aber derart wirken, dass sie sowohl erbgleiche Paare phänotypisch unähnlich machen als auch erbungleiche Paare phänotypisch ähnlicher. Ausserdem brauchen Geschwister und ZZ gar nicht in so hohem Grade erbungleich zu sein, wie das die Theorie des Aehnlichkeitsverfahrens stets behauptet ».

We consider Gottschick's criticism by no means logical and consequently untenable. Indeed, it amounts to the curious conception that on the one hand the possibility of the rise of differences or even discrepancies in taste with regard to thiocarbamides in consequence of « Umweltsverschiedenheiten » is practically denied, — Gottschick thinks it more plausible « dass nur Erbunterschiede Geschmacksdifferenzen von PTC hervorrufen » —, while on the other hand a pronounced influence of the « Umweltsverschiedenheiten » on the group of morphological traits which is used in the polysymptomatological examination, so pronounced indeed that the two members of a pair of fraternal twins show a striking external similarity, is considered quite possible.

The identity of the 2 pairs of twins examined by us cannot in our opinion be reasonably doubted; the two members of each pair were wonderfully similar in the 15 morphological traits employed. The same applies — as appears convincingly from the respective papers — to the 3 pairs of twins examined by Ardashnikov *c.s.* (2) and to the 3 pairs examined by Rife (3); it is to be noted that the former devoted a short special discussion to the usual practice of classification of twins as identicals or fraternal and were therefore quite aware of the dangers involved. So far a total of 8 cases of clear intra-pair discrepancy of taste with respect to thiocarbamides has been found on 218 pairs of identical twins. We are inclined to remark that the percentage of the cases in question is too large to be accounted for in the way proposed by Gottschick; after all it may be expected that so extreme an external similarity of the members of pairs of fraternal twins as would then have to be assumed must be extremely rare.

Besides the suddenly occurring and often very considerable variations in taste threshold concentration, *i.e.* the fact that « the taste world of any one individual is not a stable one », the occurrence of « crypto tasters » and « crypto non-tasters » strongly urges us to be very cautious in work in the field of genetics with the aid of thiocarbamides. In this connection an interesting illustration is furnished by the following fact, which was mentioned by Hartmann (20) and which, as far as can be judged, is reliable. She described a family consisting of the two definitely non-tasting parents and three children, of which only two were non-tasters, while the third was a taster,

which is apparently in conflict with the rule of heredity. This latter child was a « crypto non-taster »; its taste threshold concentration was found to be slightly lower than the « taste blindness threshold concentration », *i.e.* it lay in a concentration range where, in view of the shape of the taste threshold concentration/frequency curve, « crypto non-tasters » may doubtless be expected. Another family, examined by Levine and Anderson (21), also presented a remarkable picture, which we shall not discuss here; perhaps the father was a « crypto taster » in this case.

It may suffice here to give two explicit examples of lines of work where caution will be necessary. A test with a solution 1:5,000 of PTC or EPTC is not a really conclusive aid in the classification of twins as identicals or fraternal, or — contrary to the suggestion of Blakeslee and Salmon (22), and especially to the opinion of Cardullo and Holt (23) — for obtaining a decision in cases of doubtful paternity.

In work in the field of genetics it is advisable to use PTC, since this compound is better soluble in water than EPTC, and to perform, besides the test with the solution of the « taste blindness threshold concentration » (1:5,000), tests with solutions of somewhat higher and lower concentrations, *e.g.* in the range between 1:500 and 1:40,000. Moreover, it is desirable to repeat the tests a few times with intervals of, for example, some days.

In work of a more statistical character with large numbers of test persons — in the examination of racial differences in the occurrence of taste blindness, for instance — the appearance of « crypto tasters » and « crypto non-tasters » on the other hand is in all probability of little importance, if any. It does not seem necessary to us to expatiate on this now.

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Summary

During the World Twin Congress held at Eindhoven (Netherlands) in 1957 we tested 70 pairs of identical twins for their ability to taste *para-ethoxyphenylthiocarbamide* (EPTC). In 2 pairs a clear intra-pair discrepancy of taste was encountered. The tests with these 2 pairs were continued weekly for about six months. The result was always the same. One member of the pair found a bitter taste even in a solution 1:320,000 of EPTC; the other member considered even a solution 1:5,000 of this compound, *i.e.* a solution of the « taste blindness threshold concentration », completely tasteless. The former is a « taster », the latter is a « non-taster ».

A similar intra-pair discrepancy in taste with regard to *phenylthiocarbamide* (PTC) in pairs of identical twins has been found by Ardashnikov *c.s.* and by Rife.

The ability to taste certain thiocarbamides without doubt being a hereditary property, the discrepancy of taste found must have an exogenic cause, the nature of which is unknown.

The fact in question is discussed on the basis of the well-established bimodality of

the taste threshold concentration/frequency curve for thiocarbamides. It is pointed out that the « non-tasters » of the pairs of identical twins under consideration must be regarded as « *crypto tasters* ». Their taste threshold concentration lies on the « wrong » side of the (more or less arbitrarily adopted) « taste blindness threshold concentration » (1:5,000 for EPTC and PTC).

The consequences of the existence of « *crypto tasters* » and also « *crypto non-tasters* » for work in the field of genetics with the aid of appropriate thiocarbamides are briefly indicated.

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RIASSUNTO

Durante il Congresso Mondiale dei gemelli tenutosi a Eindhoven (Olanda) nel 1957 abbiamo esaminato 70 coppie di gemelli identici rispetto alla loro capacità di gustare la para-*etossifeniltiocarbamide* (EPTC). In due coppie fu riscontrata una chiara discordanza gustativa intracoppia. Le prove con queste due coppie furono continuate settimanalmente per circa 6 mesi. Il risultato fu sempre lo stesso. Un membro della coppia trovava un sapore amaro anche in una soluzione di 1:320.000 di EPTC; il cogemello considerava insapore anche una soluzione di 1:5.000 dello stesso composto, cioè una soluzione di « concentrazione limite di sensibilità gustativa ». Il primo era un « gustatore », il secondo un « non gustatore ».

Una simile discordanza gustativa per la *feniltiocarbamide* (PTC) in coppie di gemelli identici è stata trovata da Ardashnikov e da Rife.

La capacità di gustare certe tiocarbamidi essendo indubbiamente una proprietà ereditaria, la discordanza gustativa deve avere una causa esogena, la cui natura è sconosciuta.

La questione viene discussa in base alla ben nota bimodalità della curva concentrazione di soglia gustativa / frequenza. Si fa notare che i « non gustatori » delle coppie di gemelli identici considerati devono considerarsi come « cripto-gustatori ». La loro concentrazione di soglia gustativa si trova dal lato « sbagliato » di quella che più o meno arbitrariamente è stata adottata come « concentrazione limite di sensibilità gustativa » (1:5.000 per la PTC e la EPTC).

Vengono brevemente indicate le conseguenze della esistenza di « cripto-gustatori » ed anche di « cripto-non-gustatori » per le ricerche genetiche col sussidio di appropriate tiocarbamidi.

RÉSUMÉ

Pendant le Deuxième Congrès Mondial des Jumeaux qui a eu lieu à Eindhoven (Pays Bas) en 1957, nous avons examiné 70 couples de jumeaux identiques par rapport à leur capacité de goûter la para-*éthoxyphéniltiocarbamide* (EPTC). Chez deux couples on a trouvé une différence intra-couple bien marquée. Les examens sur ces deux couples ont été continués chaque semaine pendant six mois. Les résultats en ont été toujours les mêmes. L'un des jumeaux dans chaque couple goûtait encore amer avec une solution 1:320.000 de EPTC; l'autre jumeau considérait tout à fait insipide une solution 1:5.000 du même composé, soit une solution de « concentration de seuil de sensibilité gustative ». Le premier jumeau est un « goûteur », l'autre un « non-goûteur ».

Une différence semblable intra-couple par rapport à la capacité de goûter la *phéniltiocarbamide* (PTC) a été observée chez des couples de jumeaux identiques par Ardashnikov et par Rife.

La capacité de goûter certaines thiocarbamides étant sans doute une qualité héréditaire, la différence trouvée en ces cas doit avoir une cause extérieure dont la nature est inconnue.

La question est discutée sur la base de la bimodalité reconnue de la courbe concentration de seuil gustatif / fréquence pour les thiocarbamides. On conclut que les « non-goûteurs » des couples de jumeaux identiques étudiées sont à considérer comme « crypto-goûteurs ». Leur concentration de seuil gustatif se trouve du côté « erroné » de celle que l'on a (un peu arbitrairement) adoptée comme « concentration de seuil de sensibilité gustative » (1:5.000 pour l'EPTC et la PTC).

On indique les conséquences de l'existence des « crypto-goûteurs » et des « crypto-goûteurs » et des « crypto-non-goûteurs » pour les recherches de génétique par le moyen de thiocarbamides appropriées.